ON THE USE OF CONTRALATERAL AUDITORY SUPPRESSION OF TRANSIENT EVOKED OTO-ACOUSTIC EMISSIONS AND HEART RATE VARIABILITY TO ESTABLISH BASELINE MEASURES FOR CONCUSSION AND RETURN TO PLAY

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Abstract

Concussion injuries have gained the attention of healthcare providers because of the effects that persistent reoccurring symptoms, associated with the injury, can have on normal functioning. As such, there is a recognized need to establish appropriate pre-injury measurements of individuals at risk for concussion so that healthcare providers can establish a more accurate diagnosis, management and treatment post concussion.

The purpose of the present study was to assess the stability of heart rate variability (HRV) and contralateral auditory suppression of transient evoked oto-acoustic emissions (CAS TEOAE) as objective measures for the assessment of concussion.

The study was conducted in three phases: 1) to assess the stability of the methodologies related to measuring (n=25); 2) to determine the relationship between the clinical measures (HRV & CAS TEOAE) with psychological measures (n=75) (DASS-21 and PASS-20); 3)to assess to response profile following injury on a case study basis (n=1).

A test-retest research design was used to establish the stability of the clinical methods. Twenty-five university-aged individuals were assessed on HRV and CAS TEOAE on two separate occasions. The McNemar chi-square of symmetry was used to establish the measure of difference between day 1 and day 14, while the kappa statistic of agreement was used to assess the measure of agreement between the variables.

No significant differences were found between test-retest observations for selected measures of CAS TEOAE (Y1414, Diff14141, X2000, SUM2000) and selected measures of HRV (RMSSD and mean HR). In addition, two variables from each of the HRV test and the CAS TEOAE test showed significant agreement between the test-retest days.

As part of phase 2 significant relationships, observed independently between HRV and CAS TEOAE were quantified with subscales of the DASS-21 and PASS-20 in a cohort of university varsity athletes. Relationships with the subscale were established using the Spearman

Correlation Coefficient both within the entire sample as well as within the sub-cohorts based on concussion history. The relationships in the total population were not present in those who reported a previous history of concussion, indicating a change in psychological measures and their predictability of HRV.

In phase three, the case study of one athlete showed notable decreases in HRV (a condition of injury) and a decrease in CAS TEOAE functioning in the immediate post injury state, with a noted increase in both measures during the recovery phases. These results support the need for further study of HRV and CAS TEOAE as objective measures of concussion.

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List of Abbreviations

AV-atrioventricular
BAI-Beck Anxiety Inventory
CAS TEOAE- Contralateral Auditory Suppression of Transient Evoked Otoacoustic Emissions
CEOAE- Click Evoked Otoacoustic Emission
CV- coefficient of variance
DASS- Depression Anxiety and Stress Scale
DPOAE-distortion Product Otoacoustic Emission
ECG-electrocardiogram
FFT-Fast Fourier transformations
HF- High Frequency
HRV- Heart Rate Variability
ICC- Intraclass correlation coefficient
LF- Low frequency
n.u. - Normalized units
PANAS-Positive And Negative Affect Schedule
PASS- Pain Anxiety Symptom Scale
PCS-Post concussion syndrome
pNN50- Percentage of normal-to-normal intervals that differ by more than 50ms
PNS-parasympathetic nervous system
RMSSD- Root mean squared of the standard deviation
RR/NN-normal-to-normal interval
SA- Sino atrial
SCAT III- Sport Assessment Concussion Tool
SDNN-Standard deviation of the normal-to-normal interval
SNS-sympathetic nervous system,
SOAE- Spontaneous Otoacoustic Emission
SSOAE-Synchronized Spontaneous Otoacoustic Emission
TEOAE- Transient Evoked Otoacoustic emission
VLF- Very low frequency

Glossary of Terms

Autonomic Nervous System- the division of the nervous system that encompasses efferent neurons that synapse with and regulate the function of internal organs and other structures not under voluntary control. (Stanfield, 2013)
Basilar membrane-membrane in the cochlea of the inner ear that separates the scala tympani from the scala media (Stanfield, 2013)
Cochlea- A closed fluid filled spiral-shaped structure in the inner ear that contains the receptor cells for hearing (Stanfield, 2013)
Coefficient of variance- measures the variability of a series of numbers independent of their unit of measurement (Abdi, 2010)
Concussion- a complex pathophysiological process affecting the brain, induced by biochemical forces (McCrory, 2013)
Contralateral Acoustic Suppression of Transient Evoked Oto-Acoustic Emissions (CAS TEOAE)- the slight depression of OAE level caused by broadband noise in the contralateral ear (Kemp, 2002)
Contralateral-referring to ascending and descending pathways that are on the side opposite their origin (Stanfield, 2013)
Depression Anxiety Stress Scale (DASS)- a 21 or 43 item self report questionnaire to measure different symptoms of depression, anxiety and stress (Lovibond & Lovibond, 1995)
Endolymph- fluid found in the scala media of the cochlea, and has a high concentration of potassium ions and a low concentration of sodium ions (Stanfield, 2013)
Frequency Domain- measurement of HRV using spectral analysis to assess different measurements (Task Force, 1996)
Heart Rate Variability (HRV)- Oscillations in the interval between consecutive heart beats (Task Force, 1996)
Ipsilateral- referring to ascending and descending pathways that are on the same side as their origin (Stanfield, 2013)
Kappa z-score-a quantitative measure of the magnitude of agreement between observations (Viera & Garrett, 2005)
McNemar Chi-Square- a statistic that enables the researcher to evaluate the concordant pairs while adjusting for the discordant pairs and asses if the two sets of data are significantly different (McNemar, 1947; McNemar, 1969)
Organ of Corti-the sensory organ for sound; located on top of the basilar membrane in the cochlea (Stanfield, 2013)
Otoacoustic Emissions (OAE)- sounds that arise in the ear canal when the tympanum receives vibrations transmitted backwards through the middle ear from the cochlea. They occur as a by product of a cochlear mechanism called the cochlear amplifier (Kemp, 2002)
Outer Hair Cells- the cells with stereo cilia receptor cells for hearing and equilibrium (Stanfield, 2013)
Pain Anxiety Symptoms Scale (PASS)- a questionnaire that assesses four factorially distinct components of pain-related anxiety: cognitive, fear, escape/avoidance,

physiological. (Abrams et al, 2007)
Perilymph-fluid found in the scala vestibuli and scala tympani of the cochlea in the inner ear. (Stanfield, 2013)
Reliability- the consistency of a test or measurement (Weir, 2005)
Scala Media-fluid filled duct in the cochlea also known as the cochlear duct
Scala Tympani-fluid filled duct in the cochlea also known as the tympanic duct
Scala Vestibuli-fluid filled duct in the cochlea also known as the vestibular duct
Signal Transduction- the process by which the binding of a chemical messenger to receptors brings about a response in a target cell (Stanfield, 2013)
Stereo cilia- hair like projections on the upper surface of hair cells in the inner ear that move in response to sound vibrations or acceleration of the head (Stanfield, 2013)
Sympathovagal Balance-term used to described the dual, opposing effects of the sympathetic and parasympathetic nervous systems on the sinus node (Goldberger, 1999) and is best defined as the ratio of LF to HF (Eckberg, 1997)
Tectorial membrane-membrane in the organ of Corti in which the tips of stereo cilia are embedded (Stanfield, 2013)
Time Domain- Measurement of HRV using the normal-to-normal interval and different statistical formulae (Task Force, 1996)
Vagus Nerve- major parasympathetic nerve that originates in the medulla oblongata and innervates much of the viscera; cranial nerve X (Stanfield, 2013)
Vestibular membrane-membrane in the cochlea of the inner ear that separates the scala vestibuli from the scala media (Stanfield, 2013)
Vestibulocochlear Nerve- nerve that contains the afferents for hearing and equilibrium; cranial nerve VIII (Stanfield, 2013)

Chapter 1

Introduction

1.1 Background

Concussion and issues related to post concussion events have become prominent in North American society, specifically within cohorts of active individuals. In the past, concussions have been an accepted and common event within contact sports, especially those with frequent body contact between players or the playing environment. If the fundamental principles of participating in sport are to promote health and to inspire physical activity, then concussion injuries may compromise such participation.

Concussion, which is described as a traumatically induced disturbance of brain function, is classified as a subtype of mild traumatic brain injury (Harmon et al. 2013). Depending on the magnitude and the mechanics of the injury —a linear or rotational impact to the head or body —concussion can cause bruising, and in severe cases nerve damage, to brain tissue. This type of injury is normally transient, meaning that a concussion is not expected to persist for a prolonged period of time following the injury. The signs and symptoms of concussion can manifest immediately after an injury, but in some cases may not be observed for at least eight hours after the incident (McCrory et al. 2013). Concussion has gained attention in the media because it is not only linked to acute injury, but because it has also been linked to depression, diminished sensorimotor

functioning, and early stage dementia, among athletes (Cantu, 2007; Guskiewicz et al, 2005).

As concussion injuries become prominent in the popular media and are the cause of persistent reoccurring symptoms which detract from proper functioning, the diagnosis, management and treatment of concussed athletes has gained increasing attention. Moreover, recognizing the relevance of the concussion injury on long-term consequences following involvement in sport has mediated the process of return to sport decision making among officials, coaches and players across the spectrum of physical activity.

1.2 Purpose

The present study measured the relationships between baseline estimates of physiological and neuropsychological functioning that may be influenced by concussion injury. Specifically, the primary purpose of the present study is to investigate the test-retest reliability of heart rate variability (HRV) and contralateral auditory suppression of transient evoked oto-acoustic emissions (CAS TEOAE) as objective measures to assess concussion. The secondary purpose of the present study is to evaluate the psychological measures from the PASS-20 and DASS-21 for relationships with the objective measures of HRV and CAS TEOAE as predictive variables

Finally, the present study sought to evaluate the case study response profile for a university aged varsity athlete on the objective measures of HRV and CAS TEOAE. Within this aim we, provide case study comparisons for athletes that were concussed or were suffering post concussion syndrome, to determine their recovery profile, in relation

to the injury—recovery hypothesis (Appendix A). Montelpare developed the injury recovery hypothesis in 2013. It depicts the change in a multi modality baseline assessment following a concussion injury. The key to the injury recovery hypothesis is the instability in the first few days following injury and the subsequent return to or near baseline scores. The purpose of the injury recovery hypothesis is to asses the time, in days, to return to baseline for HRV and CAS TEOAE following concussion, compared to other concussion testing methods.

1.3 Rationale

Current concussion testing methods which include the balance error scoring system (BESS), the sport concussion assessment test (version 3; SCAT3), and various neuropsychological tests (McCrory et al, 2009) are currently used following the suspected concussion injury to assess and establish quantitative estimates of the injury. Such methods have been tested and shown to be statistically stable in selected cohorts of non-concussed healthy individuals (Lovell et al. 2006), but with several limitations (McCrory et al, 2009). For example, Valovich Perrin & Gansneder (2003) identified a practice effect in participants with repeated administration of the BESS, and McCrory and coworkers indicated that the BESS has limited capacity to identify postural stability deficits only up to 72 hours following an injury (2009). A modified version of the BESS is recommended for use in the SCAT-3. However, the test is limited to testing balance on a flat surface, and no intra-rater or inter-rater reliability has been established for this modified use of BESS (Harmon et al, 2012).

Likewise, neuropsychological testing also has demonstrated limitations. Symptom reporting is a determining factor in return to play decisions. However, symptom resolution may not always indicate neurocognitive recovery (Harmon et al, 2012). Previous research by McCrea et al, showed that athletes were unwilling to report concussion symptoms; 40% of athletes felt that they were concussed but didn't report the injury. The common reason for non-reporting was attributed to the belief that they would lose playing time (McCrea et al, 2004). Johnson, Kegel & Collins (2011) identified that both extrinsic and intrinsic factors including fatigue, distractions, mood disorders and history of concussion, can influence scores on neurocognitive tests and symptom reporting.

In most sports environments the typical baseline test for concussion is the neuropsychological test. It is therefore suggested that subcortical tests which measure neural processing activity of specific cranial nerves and efferent nerve innervations of the outer auditory hair cells will provide more precise and robust estimates that are stable for detecting and tracking the concussion condition. The use of subcortical tests as used in the present research study do not require the participant's active input or extended time commitments. Specifically HRV and CAS TEOAE as non-invasive, objective measures for vagal and auditory nerve activity is hypothesized to be a more comprehensive approach that we will lead to more accurate testing methods and return to play analysis, but eliminating self-reporting of symptoms and manipulation of testing. The cranial nerve

pathways that will allow this assessment are outlined in depth in the review of literature in chapter 2.

1.4 Research Hypothesis

Heart rate variability and contralateral auditory suppression of transient evoked oto-acoustic emissions will be assessed in three stages, first for stability, secondly against psychological measures of the Depression Anxiety and Stress Scale (DASS-21) and the Pain Anxiety Symptom Scale (PASS-20) for emotional interactions and finally on a case study basis to assess the injury response profile following a concussion.

1. It is hypothesized that HRV and CAS TEOAE will be stable measurements as assed by different variables for each test respectively.
2. It is hypothesized that there will be a statistical relationship between CAS and HRV, and between HRV and DASS-21, and between DASS-21 and PASS-20. It is expected that there will be no relationship between CAS and DASS, and CAS and PASS-20.
3. It is hypothesized that there will be a significant difference between a healthy university aged score and a concussed score on HRV and CAS TEOAE.

Chapter 2

Literature Review

This section will first explore HRV and CAS TEOAE as objective measures of cranial nerve activity Then, background information on concussion and the potential use of HRV and CAE TEOAE to evaluate concussion will be presented, followed by the explanation of the DASS-21 and PASS-20 as potential relationships with the objective measures.

2.1 Heart Rate Variability

The physiological phenomenon of heart rate variability (HRV) is defined by the European Society of Cardiology and by the North American Society of Pacing Electrophysiology as an oscillation of the intervals between consecutive heart beats (Task Force, 1996). HRV is considered a clinically relevant predictor of cardiac dynamics and potential indicator for sudden cardiac death. Hon and Lee (1965) first noted the clinical relevance of HRV by measuring the changes in beat-to-beat intervals as a precursor to fetal distress. HRV has since been used as an analytical tool for patients with chronic heart failure, hypertension, diabetes, and cardiac transplantation (Task Force, 1996; Bravi, Longtin & Seely, 2011; Valencia et al, 2009). HRV has also been suggested as a clinical tool in assessing the severity mild traumatic brain injury-concussion (Goldstein et al, 1998; Lagos, Bottiglieri, Vaschillo & Vaschillo, 2012). The reason for using HRV in this application will be described in the following sections as it pertains to it's indirect measurement of vagal tone and the application of vagal tone on health outcomes.

2.1.1 Measurements

Measurements for HRV are divided into two domains, the time domain and the frequency domain. Typical variables used in the assessment of HRV are listed in Table 3.1. Despite the mathematical simplicity in the analysis of both time domain and frequency domain assessments, the measures of HRV are considered useful in clinical applications (Bravi, Longtin & Seely, 2011).

Frequency domain measurements are derived using fast Fourier transformations (FFT) and autoregressive modeling (Task Force et al, 1996, Tarvainen et al, 2013). Based on the frequency domain measurements there is power spectral analysis. Power spectral analysis is divided into the following bands: very low frequency (VLF) ranging from 0.003 Hz to 0.04 Hz, low frequency (LF) ranging from 0.04 Hz to 0.15 Hz and high frequency (HF) ranging from 0.15Hz 0.4 Hz. Frequency domain measures are reported in ms^2 (Task Force, 1996; Bravi, Longtin & Seely 2011; Nunan et al, 2009). Low and high frequency HRV measures can also be reported in normalized units (n.u.). Normalized units emphasize the two aspects of the autonomic nervous system: SNS and PNS. Normalized units provide a quantitative estimate of the balance between sympathetic and parasympathetic activity (Task Force, 1996; Nunan et al, 2009). Kubios (Finland) is a university based research group, which provides free software to estimate HRV across frequency and time domains. In particular the Kubios software uses a spectral analysis based on Welch's periodogram and autoregressive modeling. The spectrum estimates are obtained by averaging the FFT of five-minute segments within a series of cardiac cycles (Tarvainen et al, 2013). Using a short-term (five minute) analysis the researcher can

interpret total power (VLF+LF+HF) as a descriptive measure of HRV dynamics. However, it is recommended that VLF as a single measure is inconclusive and should not be used to describe HRV dynamics (Task Force, 1996; Nunan et al, 2010). Frequency domain measurements are associated with sympathetic and parasympathetic drive, which causes the HRV response. The LF band has been associated with both sympathetic and parasympathetic drive, whereas the HF band reflects cardiac vagal control (parasympathetic activity) and is associated with respiratory rhythm (Task Force, 1996; Moak et al, 2008, Nunan et al, 20010; Zhang, 2007). From the power spectrum analysis the ratio of LF to HF is also computed. The computation of the LF/HF ratio is of critical importance as it is the measure, which is used to quantify the sympathovagal balance (Task Force, 1996; Eckberg, 1997; Pagani et al, 1997).

Time domain measurements are based on the normal ECG tracing of a series of cardiac cycles. One measure is the normal-to-normal (NN) interval, which is the distance between consecutive R waves in a normal PQRS tracing. The R wave represents the long wave of ventricular contraction and is representative of the electrical activity required for ventricular ejection. Ventricular ejection fraction is driven by metabolic needs, and therefore will adjust to sympathetic, parasympathetic and hemodynamic loading in normal physiological functioning (Stanfield, 2013). Several measurements are derived from the computation of the NN interval including the mean heart rate (HR) and the mean time between each beat (represented as the mean RR). Time domain measurements are derived from the statistical evaluation of the ECG tracing for example the standard

deviation of the NN interval (represented as the SDNN) reflects the cyclic components of variability and is an indicator of overall HRV (Task Force, 1996). The root mean square of the standard deviation (represented as RMSSD) evaluates the mean squared difference of successive NN intervals and is associated with indications of parasympathetic outflow (Task Force, 1996; Kleiger, Stein, Bosner & Rottman, 1992). RMSSD is highly variable and suspect to changes based on age and physical training (Ori, Weiss, Sayhouni; Singer, 1992; Puig et al, 1993). The proportion of NN intervals differing by more than 50ms divided by the number of total NN intervals, known as the pNN50, estimates high frequency variations in heart rate and is considered a good overall indicator of HRV (Task Force, 1996). Combining frequency and time domain measurements provides a comprehensive assessment of HRV (Bravi, Longtin & Seely, 2011; Task Force, 1996; Eckberg, 1997).

Despite the ability of theses measures to assess HRV, there exists an intrinsic problem with overall HRV measurement. HRV is a measure of variance and therefore both intra-individual and interindividual comparisons may not be stable in successive trials (Fagard, Pardaens & Staessen, 1999). According to Bravi, Longtin & Seely (2011) it may be more accurate to assess HRV within an individual rather than between individuals to ensure accurate assessments. It should also be noted that there are sex, age and exercise specific differences in HRV measurements. In a retrospective study conducted by Zhang (2007) the researchers observed that heart rate, RR interval, HF, LF norm, HF norm and LF/HF were each significantly different between males and females.

Nunan et al (2010) also noted a similar difference across sex with females demonstrating lower values in RMSSD, while males had lower LF and HF values. It was also noted that with increasing age there was a concomitant decrease in total power, LF and HF measures (Zhang, 2007). Highly trained individuals showed increased values of cardiac vagal modulation including mean HR, HF, and RR interval (Puig et al, 1993; Shin et al, 1997; Sandercock, Bromley & Brodie, 2005)

Heart rate variability has also been used to as a research tool with psychological assessment. Sympathetic and parasympathetic adjust to mediate emotional coping and are the controlling factors for HRV. Physical and mental stress has an influence both of these systems with an increase in sympathetic drive and a decrease in parasympathetic control (Hughes & Stoney, 1999; Visnovcova, Calkovska & Tonhajzerova, 2013). In a stressful situation the sympathetic nervous system is activated and an increase in catecholamine release leads to an overall increase in heart rate (Gorman & Sloan, 2000), changing the HRV measurements. Stress, depression and pain are all thought to have similar effects on HRV, specifically a decreased on HF as is a measure of parasympathetic activity (Hughes & Stoney, 1999; Task Force, 1996). Hughes & Stoney found that participants scoring higher on the Beck Depression Index had significantly different HF responses to stress than their matched controls with lower scores (2000). Tousignant-Laflamme and coworkers found that males and females showed different heart rate response as a response to pain, where a positive relationship between pain and anger existed in males but was not statistically significant in females (Tousignant-LaFlamme, Rainville &

Marchand, 2005) It has also been shown that HRV is positively associated with pain (Appelhans & Leuken, 2006). Stress has also been associated with HRV (Sloan et al, 1994) and patients with anxiety disorder had lower HF at rest and during worry than a control group (Thayer, Friedman & Borkovec, 1996). Dishman and coworkers also noted an inverse relationship between HRV and recent stress (Dishman et al, 2000).

2.1.2 Sympathovagal Balance

The sympathetic nervous system (SNS) and parasympathetic nervous system (PNS) regulate the cardiac cycle. Having two opposing systems allows the cardiac cycle to adapt to intrinsic and extrinsic changes in stressors in the body and maintain homeostasis. The SNS regulation of cardiac output via the sympathetic cardiac nerve, stems from thoracic nerves T1- T4, and has receptors in the sino atrial node (SA node), atrioventricular node (AV node) and the ventricular myocardium (Stanfield, 2013). The SNS regulation is activated and maintained by the release of epinephrine and norepinephrine followed by a signal cascade that results in an acceleration of diastolic depolarization (Stanfield, 2013 &Task Force, 1996) resulting in an increased heart rate consistent with the 'fight or flight response'.

PNS regulation arises from the vagal nerve and has receptors in the SA node and in the AV node (Stanfield, 2013). PNS regulation is controlled by the vagal nerves release and complete expression of acetylcholine and results in a slow diastolic depolarization (Task Force, 1996; Eckberg, 1997). Consistent with the 'rest and digest' response, parasympathetic and vagal tone is high in resting conditions (Goldberger,

1999). The regulation of the cardiac cycle is a result of the balance between the SNS and the PNS, through the vagal nerve, termed sympathovagal balance. It is commonly accepted and understood that efferent vagal activity can be indirectly quantified with spectral analysis of the high frequency band, from 0.4Hz-0.15Hz, elaborated on below (Task Force, 1996; Berntson et al, 1997; Pagani et al, 1997). However, the quantification of SNS in HRV activity is less accepted and more controversial. It is argued that the low frequency band (0.04-0.15Hz) reflects SNS regulation of the SA node (Berntson et al, 1997) or a combination of both SNS and PNS (Task Force, 1996; Goldberger, 1997). The relationship of SNS and PNS, the sympathovagal balance, can be shown through the LF/HF ratio or the average RR interval which is ventricular depolarization, or the mean time between each beat of the heart.

2.2 Otoacoustic Emissions

Otoacoustic emissions (OAE) are physiologically produced response to sound when the tympanum receives vibrations backwards from the cochlea through the middle ear(Kemp, 2002). OAEs originate from the cochlea outer hair cells and reflect back through the middle ear and ear canal, as a by-product response from the cochlear amplifier (Kemp, 2002). It is important to understand that OAE measurement is not a test of hearing; it is a test of cochlear and peripheral auditory system function (Kemp, 1978; Kemp 2002). The OAE response is a pre-neural cochlea response, as the basilar membrane of the cochlea vibrates in response to sound waves. These sound waves are then sent back through the ear canal is a result of the reflection of a sound wave from the

outer hair cells in the cochlea and are considered a naturally occurring imperfection (Abdala & Visser-Dumont, 2003; Kemp, 2002). The hearing pathway as described by Standfield (2013) presented below in Figure 2.1 explains the signal transduction of a sound wave and it interactions with the cochlea, and specifically the organ of Corti and the outer hair cells.

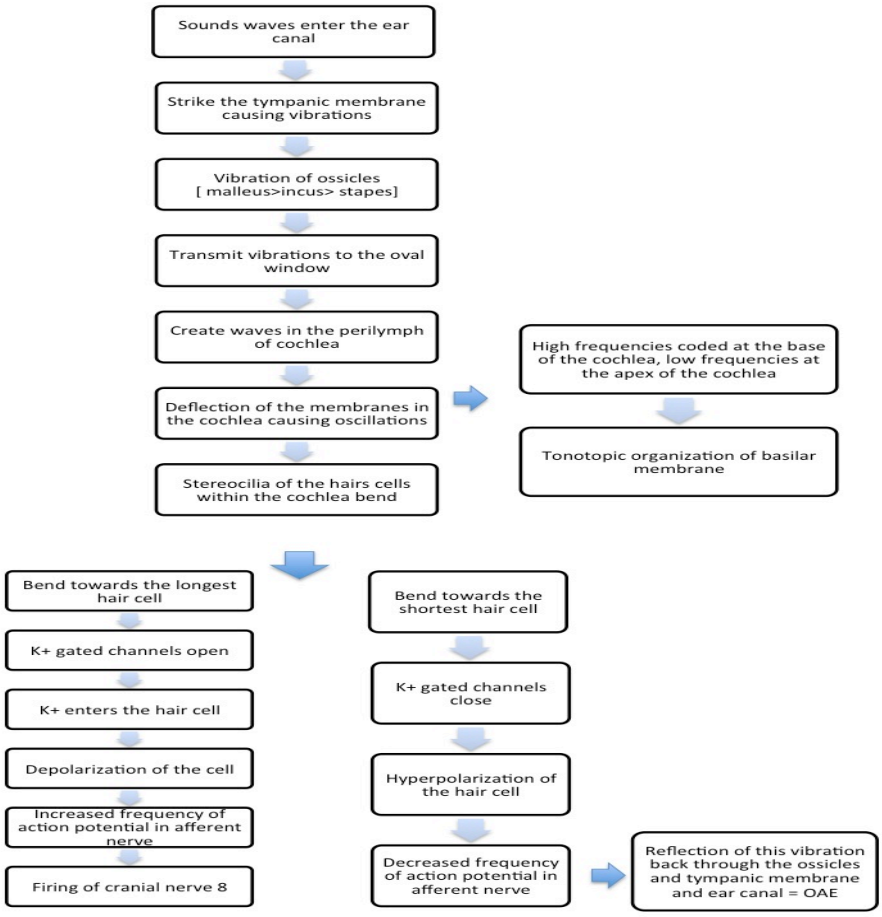

Figure 2.1 Hearing Pathway described from Stanfield (2013).

The OAE arises as a reflection of the oscillations from the traveling sound wave of the basilar membrane and the bending of the outer hair cells of the organ of the Corti. The OAE reflects back through the ossicles, tympanic membrane and then the ear canal where it can be picked up by a very sensitive microphone (Kemp, 2002; Stanfield, 2013).

2.2.1 Distortion Product and Transient Evoked Otoacoustic Emissions

In the field of OAE research, there are two main testing mechanisms for evoking the OAE response: the distortion product (DPOAE) stimuli and the click or transient evoked (TEOAE) stimuli. A DPOAE test uses two different pure tones (f1, f2) that are presented in the ear canal at the same time (Abdala & Visser-Dumont, 2003). The DPOAE technique is more suited for advanced clinical uses o, but the analysis is complex leading to difficulties in interpreting results (Kemp, 2002) Comparatively TEOAEs are tested using one non-linear click stimulation at multiple frequencies (Hatzopoulos, Pertucelli, Morlet & Martin, 2003). The TEOAE technique is more sensitive to cochlear changes that are quantifiable by the waveform response and is primarily recorded in the speech frequency range of 1 to 4 kHz (Kemp, 2002).

2.2.2 Spontaneous Otoacoustic Emissions

One type of imperfection of the cochlear OAE response is a spontaneous OAE (SOAE). Spontaneous OAE are essentially when a pure tone is produced in the absence of a stimuli and it arises from positive feedback of a traveling sound wave (Abdala & Visser-Dumont, 2003). The positive feedback leads to self-oscillation and wave energy, which would typically be absorbed, that stimulates the outer hair cells leading to an

unprovoked OAE (Kemp, 2002). The recording of SOAEs is well recognized and mechanisms for their function in agreed upon. However, the exact effect they have on the recording of DP or TEOAEs is not entirely understood (Bright, 2002; Killan, Lutman & Montelpare, 2011). It has been hypothesized that SOAEs play a role in tinnitus or can be perceived as tinnitus, which would give further insight into its clinical relevance, but it has not been definitively investigated (Chery-Croze, Truy & Morgan, 1994; Kemp, 2002).

2.2.3 Contralateral Acoustic Suppression of Transient Evoked Otoacoustic Emissions

Previous research has established that the TEOAE response is suppressed (i.e. the linear amplitude of the response is decreased) by the presence of contralateral broadband (high frequency) noise (Collet et al, 1990; Hood et al, 1995). This process is referred to as the contralateral acoustic suppression of TEOAE (CAS TEOAE). The process occurs in individuals who demonstrate a properly functioning auditory nerve pathway. Collet and coworkers (1990) hypothesized that the suppressive effect could evaluate the efferent nerve pathway and its function. Kemp (2002) suggested that the significance of the presence and absence of the contralateral suppression response may clarify neural audiological pathologies (Harkrider & Bowers, 2009).

The mechanism of contralateral suppression is facilitated by the olivocochlear reflexes (lateral and medial) of both the ipsilateral and contralateral ears: where ipsilateral is defined as when the ascending and descending pathways are on the same side as their

origin, i.e. the ear being tested with TEOAE, and contralateral as when the ascending and descending pathways are on the opposite side as the origin, i.e. the untested ear (Stanfield, 2013). There are two main hypotheses about the exact mechanism of contralateral suppression presented by Giraud et al (1995). They hypothesized that the acoustic reflex leads to the contraction of the stapedius muscle and that will decrease the OAE response, or that contralateral suppression involved direct cochleo-cochlear interaction via efferent nerve pathways (1995). Testing various populations with various auditory impairments the concluded that the medial olivocochlear pathway is involved in contralateral suppression, as suppression persisted in participants with Bell's Palsy, where the middle ear reflexes are lost, but not in participants with vestibular neurotomy, where the olivocochlear fibres are cut (Guiard et al, 1995).

As stated above, when the outer hair cells bend in response to oscillation of the organ of the Corti, hyperpolarization of the hair cell leads to neurotransmitter release in the inner hair cell and the action potential in the auditory nerve (Stanfield, 2013). The medial olivocochlear bundle synapses directly into the outer hair cells, and the wave stimulation activates an OAE and the efferent nerve pathway. When this happen simultaneously in the ipsilateral and contralateral ears, the stimulus in the contralateral ear will travel the medial olivocochlear pathway and suppress the OAE in the ipsilateral ear (Murdin & Davies, 2008). This type of suppressive effect has been shown in all three types of OAEs mentioned above, DPOAE (Guinan, 2006), TEOAE (Collet, Veuillet, Bene & Morgan, 1992) and SOAE (Mott, Norton, Neely & Warr 1989).

To best record the suppressive effect the clinical testing has used TEOAE, as it is easier to facilitate at one frequency compared to the two frequencies used for DPOAE testing (Murdin & Davies, 2008) However, there has been reported large interindividual and intra-individual variability in term of suppression values of TEOAEs (Collet et al, 1994; Giraud et al, 1995; Murdin & Davies, 2008). Giraud and co workers found mean suppression values of TEOAE in healthy individuals to be 2.47 dB (SD1.67 dB) (1995). De Ceulaer et al found a mean suppression of TEOAEs to be 1.52 dB (SD 1.09) at a stimulus level of 12 dB threshold (2001). Murdin & Davies reported a normal suppression cut off to be 0.7 dB (2008). The effect of subject task during the testing for contralateral suppression has also been noted by De Boer & Thornton, where participants who focused on arbitrary tasks, such as reading or watching a muted video rather than focusing on the presented stimulus had higher suppression scores (2007). Harkrider & Bowers also reported on this phenomenon, when attention was paid either the ipsilateral or contralateral stimulus the suppression was reduced in normal hearing adults (2009).

2.3 Concussion

Concussion is a type of mild traumatic brain injury that involves a complex physiological process affecting the brain (Harmon et al, 2012; McCrory et al, 2013). Concussion can be caused by a direct blow to the head or neck, or an indirect blow to the body causing force on the head (McCrory et al, 2013). Concussion is a rapid onset injury that can have symptoms appearing either immediately or after several hours or even days following the injury. Concussion is also described as a transient injury, because it is not

expected to last for a prolonged period of time (Harmon et al, 2012). There are several symptoms associated with concussion including nausea, vomiting, headache, dizziness and sensitivity to noise and light. Loss of consciousness is generally thought to coincide with concussion, however it is not a necessary condition of concussion as noted by Guskiewicz, Weaver, Padua & Garrett who indicated that as high as ninety percent of concussions do not results in loss of consciousness (2000).

Reports of concussion have become more widespread in the media, and therefore the diagnosis and treatment of concussion has become a growing field. The standard post injury assessment is called the Sport Concussion Assessment Tool, or SCAT III, developed from the 4th annual Consensus Meeting on Concussion in Sport (McCrory et al, 2013). The SCAT has a variety of assessment tools including a symptom reporting scale, immediate memory test, modified balance error scoring system (BESS), cognitive assessment, Maddock score, and the Glasgow coma scale. The SCAT version 3 is suitable for youth's aged 13 and over (McCrory et al, 2013). One difficulty with concussion diagnosis is the unwillingness of athletes reporting their injuries. McCrea, Hammeke, Olsen, Leo & Guskiewicz noted that forty percent of concussed athlete failed to report their injury (2004). Further, many athletes report symptoms they may not realize are associated with a concussion (Delaney, Lacroix, Leclerc & Johnston 2002). Lovell et al reported that healthy women report more symptoms than healthy men at baseline (2006). The reluctance of athletes to report symptoms and especially those related to concussion is a problem as its diagnosis and return to play protocol is reliant on

symptom reporting. A more objective measure of concussion and recovery could help eliminate the weight on symptom reporting as a diagnostic tool.

There is also an importance in accuracy of baseline testing, as there are several confounding factors including sex, age, sport type, and previous medical conditions that make sideline testing difficult without a baseline value to compare to (Harmon et al, 2013). The return to play protocol outlined by Harmon et al (2013) and McCrory et al. (2013) is an individual approach where the athlete needs to be asymptomatic at rest, before beginning a gradual increase in physical activity. If at any point during the return to activity the athlete becomes again symptomatic the athletes must wait until he or she is asymptomatic and then begin the process again. Having an athlete return to play before completing the gradual return to play protocol, or while they are still symptomatic puts them at risk for second impact syndrome. Although second impact syndrome is rare, it involves a second blow to the head, or concussion, before the previous concussion is completely healed or repaired and can be fatal (Bey & Ostick, 2009). Therefore proper return to play monitoring is crucial.

Concussion is a prevalent injury in the sporting community. In a three-year retrospective analysis across ten different sports mild traumatic brain injuries accounted for 5.5% of total injuries (Powell & Barber-Foss, 1999). American football has the highest prevalence of concussion (Powell & Barber-Foss, 1999) and across sports female athletes are at a higher risk than males in the same sports (Dick, 2009). For example: female soccer and basketball players are at a significantly higher risk compared to their

male counterparts based on reported concussions from the NCAA (Covassin, Swanik & Sachs, 2003). It is also noted that there is a higher incidence of reported concussion in game situations compared to practice regardless of sex or sport (Covassin, Swaink, & Sachs, 2003)

2.3.1 Concussion and Heart Rate Variability

Goldstein et al first presented early evidence of a relationship between mild traumatic brain and cardiac dynamics injury in 1998. These researchers showed that concussion injury had an adverse effect on the electrophysiology of the coronary system. Specifically they found an inverse association between heart rate and a neurological injury, which demonstrated direct effects between the autonomic nervous system and cardiovascular dynamics. This finding prompted more research into the apparent relationship between concussion and HRV.

Gall, Parkhouse & Goodman (2004) measured HRV using the frequency domain variables in concussed participants versus a group of age-matched controls, while at rest and during a short exercise test. They found no significant difference in any of the variables at rest, but reported a statistically significant difference in the RR interval, high frequency and low frequency during exercise when concussed participants were compared to controls (Gall, Parkhouse & Goodman, 2004). They also concluded that patients with sport related concussions recovered within seven to ten days of the injury while non-athletes could require up to three months to recover. The decline in LF and HF values was consistent with the findings Goldstein et al (1998). La Fountaine, et al (2009)

used approximated entropy (ApEn) based on the evaluation of the signal from the ECG t describe cardiac dynamics. In a subsequent study La Fountaine et al (2011) investigated the variability of successive QT intervals in concussed participants versus matched controls. Although the researchers observed a higher QT interval 48 hours following injury, there was no statistically significant difference in the concussed participants and their matched controls. However, La Fountaine's studies evaluated 3 concussed participants each, leaving room for large variability and decreased testing power (La Fountaine, Gossett, De Meersman & Bauman, 2011). All researchers concluded the link between cardiovascular functions, autonomic nervous system and concussion existed but with such small sample sizes it was difficult to infer theses results to a larger population.

Lagos, Bottiglieri, Vaschillo & Vaschillo (2012) has suggested the role of HRV and biofeedback training in patients whose concussion injury did not resolve in the short term, also known as post concussion syndrome (PCS). The decreased ability for the body to regulate HRV on its own post concussion injury as noted by Dewitt and Prough (2003) through increased SNS activity could be used to mediate recovery protocols in patients with PCS.

Theses studies are important in that they support the notion that HRV can provide information about cardiac dynamics with regard to concussion recovery and return to play decisions for athletes.

2.3.2 Concussion and Audiological Measures

The use of audiological measures in the diagnosis and treatment of concussion is a very new idea, especially as it pertains to sport related concussion. However, audiological measurement has been established for a population of war veterans who have suffered mild traumatic brain injuries (mTBI) in the line of duty. The most common symptom of neurological dysfunction in veterans is tinnitus, or the persistent ringing of ones ears. Lew, Jerger, Guillory & Henry found that in 252 patients suffering mTBIs 38% reported tinnitus (2007). In a study done by Oleksiak et al. of veterans suffering audiological symptoms following an mTBI, of the 21 DPOAEs tested 81% were abnormal or absent (2012). The Oleksiak research team went on to recommend OAE testing as a way to evaluate sensorineural or subclinical hearing loss (2012). In a case study by Cevette and Bielek (1995) investigated the use of TE and DPOAEs, they also concluded that OAE measurement added a new dynamic to brain injury assessment. Cercanic, Prasher, Raglan, & Luxon tested participants with persistent tinnitus and other auditory symptoms following a head injury (1998). They found higher rates of SOAEs and reduced suppression in those participants with head injury compared to matched healthy controls (Ceranic et al, 1998). Nolle, Todt, Seidl & Ernst noted complete loss of the stapedius reflex in almost half of their participants following a head injury (2004).

When using OAE measurement to evaluate any type of disturbance or injury, it is important to note a sex difference. It is well established that SOAEs are more frequent and stronger in females and that TEOAEs are stronger in females as well (Bilger, Matthies, Hammel & Demorest, 1990; McFadden, 1993, McFadden, 1998; McFadden,

Martin, Stagner & Maloney, 2009). There is asymmetry reported in the presence of SOAE and TEOAEs where the response is greater in the right ear than the left (Bilger, Matthies, Hammel & Demorest, 1990; McFadden et al, 2009). It is also noted that there is higher interindividual variability with OAE recordings, DP or TE, but that intra-individual differences, i.e. left and right symmetry should be very similar (Kemp, 2002).

2.4 Psychological Measures

2.4.1 Pain Anxiety Symptoms Scale

The Pain Anxiety Symptoms Scale-20, (PASS-20) (McCracken and Dhingra, 2002) is a 20-item scale measuring aspects of fear of pain and pain coping. It is the short version of the original full length 40-question Pain Anxiety Symptom Scale (PASS) developed by McCracken, Zayfert & Gross (1992). The original survey and the short version can be broken into 3 response categories cognitive, physiologic and motoric that are represented by four subscales; cognitive anxiety, escape/avoidance, fear and physiological anxiety (McCracken, Zayfert & Gross, 1992). The cognitive anxiety subscale assess experiences of pain as it manifest in cognitive symptoms i.e. “I feel disoriented and confused when I hurt”. The PASS-20 has been shown to highly correlate with the cognitive and somatic subscales of the Cognitive Somatic Anxiety Questionnaire (CSAQ; McCracken, Zayfert & Gross, 1992). The escape/avoidance subscale assesses behavioural responses to pain i.e. “ I try to avoid activities which cause pain”. The escape/avoidance subscale has been correlated with the McGill Pain questionnaire and its

affective subscale (Burns et al, 2000; McCracken, Zayfert & Gross, 1992) and the Pain Behaviour checklist avoidance subscale (McCracken, Gross, Aitken & Carnrike, 1996) The fear subscale assesses the fearful response to pain either experienced or anticipated i.e. “I dread feeling pain”. This subscale has been correlated to the physiological anxiety subscale assessing symptoms relating to somatic arousal i.e. “I become sweaty when in pain”. All of the questions in the survey are ranked on a scale from 0 (meaning never) to 5 (meaning always) (McCracken, Zayfert & Gross, 1992; McCracken & Dhingra, 2002). Clinical and nonclinical patients data can be found in Table 2.1.

Table 2.1. Data from a clinical and nonclinical population for the PASS-20

	Abrams, Carleton & Asmundson, 2007 Nonclinical	McCracken and Dhingra, 2002 Clinical
Cognitive	9.0 ±5.2	12.3±6.7
Escape/Avoidance	6.4±3.8	12.8±6.1
Fear	4.1±3.7	7.4±6.4
Physiological Anxiety	4.6±4.0	6.2±5.7
Total	24.0±13.5	38.6±20.4

For the purpose of this research the main subscale of interest will be physiological anxiety as it pertains to physical manifestations of pain such as increased heart rate, dizziness and difficulty relaxing (McCracken & Dhingra, 2002). In the initial study to construct the PASS-20, it was found to be a suitable alternative for the long form 40

question PASS; McCracken & Dhingra concluded that the shortened form is a valid alternative for the original (2002).

2.4.2 Depression Anxiety and Stress Scale

The Depression Anxiety and Stress Scale (DASS; Lovibond & Lovibond, 1995) is a 42-item scale measuring depression, anxiety, and stress symptoms. The DASS exists as a public domain survey in two forms, the full length 42 questions versions, and a short form 21 question version (DASS-21). Both versions were created by Lovibond & Lovibond (1995). The DASS and DASS-21 are ranked on a scale from 0-3, where 0 means "did not apply" and 3 means "applied to me very much". The *Depression Scale* assesses dysphoria, hopelessness, devaluation of life, self-deprecation, lack of interest/involvement, and inertia i.e. "I felt downhearted or blue". The *Anxiety Scale* assesses autonomic arousal, skeletal muscle effects, situational anxiety, and subjective experience of anxious affect i.e. "I was aware of dryness in my mouth". The *Stress Scale* is sensitive to levels of chronic non-specific arousal: it assesses difficulty relaxing, nervous arousal, and being easily upset/agitated, over-reactive and impatient i.e. "I felt it hard to wind down"(Lovibond & Lovibond, 1995). Each subscale has 14 questions or 7 questions for the original and short form respectively. The maximum possible overall score is 120 and 61 respectively, indicating higher markers of depression, anxiety, and stress with higher scores. The DASS manual includes a scoring section where each scale response total is given a ranking from "normal" to "extremely severe". Normative scores for clinical and non-clinical patients have been established and are available in Table 2.2.

Table 2.2
Normative and clinical data for the DASS and DASS-21

	Lovibond & Lovibond, 1995 DASS	Antony et al, 1998 DASS	Antony et al, 1998 DASS-21	Henry & Crawford, 2005 DASS- DASS-21
Depression	Normal 0-9 Mild 10-13 Moderate 14-20 Severe 21-27 Extremely Severe 28+	Nonclinical- 2.2 ±2.8 Panic Disorder- 12.8±9.5 OCD-13.4 ±11.5 Major Depressive Disorder- 29.78.4 Social Phobia-13.2±8.9	Nonclinical-2.1±3.6 Panic Disorder- 12.8±10.2 OCD-13.311.8 Major Depressive Disorder-30.0±9.2 Social Phobia-13.2±9.3	DASS- 5.6±7.5 DASS-21-2.8 ±2.9
Anxiety	Normal 0-7 Mild 8-9 Moderate 10-14 Severe 15-19 Extremely Severe 20+	Nonclinical-1.4±1.9 Panic Disorder- 16.3±10.0 OCD-8.86.7 Major Depressive Disorder-12.9±8.7 Social Phobia- 11.2±8.9	Nonclinical-1.2±1.8 Panic Disorder- 18.710.8 OCD-9.3±7.6 Major Depressive Disorder-14.0±9.8 Social Phobia- 12.2±10.2	DASS- 3.6±5.4 DASS-21- 1.9±3.0
Stress	Normal 0-14 Mild 15-18 Moderate 19-25 Severe 26-33 Extremely Severe 24+	Nonclinical- 4.1± 3.8 Panic Disorder- 20.3 ±10.8 OCD- 17.6±10.8 Major Depressive Disorder-25.5± 9.0 Social Phobia-17.1 ±10.4	Nonclinical-3.5±3.9 Panic Disorder- 20.0±11.6 OCD-17.61±1.0 Major Depressive Disorder-24.3±9.8 Social Phobia- 16.61±0.9	DASS- 9.3±8.0 DASS-21- 4.7±4.2
Total	Normal 0-78 Mild 78-87 Moderate 87-95 Severe 95-98 Extremely Severe 98+			DASS- 18.4±18.8 DASS-21- 9.4±9.7

This scoring model can be used for the DASS-21 by simply multiplying the total score in each subscale by 2. In further analysis of the DASS scores, Crawford & Henry concluded that the survey is not influenced by gender, occupation, education or age (2003).

The DASS-21 was created primarily for easier clinical use, quicker administration and a cleaner factor structure (Antony et al, 1998). It possesses high construct validity and reliability and is therefore an accurate representation of the original DASS (Antony et al, 1998; Henry & Crawford, 2005). The DASS has shown to correlate with several different measures of depression, anxiety and stress. The Beck Depression Inventory (BDI) is correlated highly with the depression subscale of the DASS and the DASS-21 (Antony et al, 1998; Lovibond & Lovibond, 1995), and inversely correlated with positive activity portion of the Positive And Negative Affect Schedule (PANAS; Henry & Crawford, 2005). The anxiety subscale is highly correlated to the Beck Anxiety Inventory (BAI)

Chapter 3

Methodology

A three-phase approach was used to evaluate CAS TEOAE and HRV. The first phase was intended to establish test-retest stability. The second phase evaluated the interactions between the baseline testing values of the objective measures of CAS TEOAE and HRV with the psychological measure of DASS-21 and PASS-20. The final phase evaluated a case study of a concussed varsity athlete at baseline and following injury.

3.1 Ethics Approval

The project was approved by the UPEI Research Ethics Board. Each participant provided written informed consent to participate. Participants under the age of 18 did not complete this project, as additional consent would have been required.

3.2 Anonymity and Confidentiality

For the benefit of the participants in this research project an individual identification number was used in place of names. Only the research team had access to the names and numbers of the individual participants. Where a participant was not a UPEI student a seven number ID was generated consisting of year/month/0xx i.e. 1401001. Once the data were collected and stored in the secure database, each data entry was only identifiable by the assigned or generated ID number. Participants all signed a

letter of informed consent before participating in the study. The letter of consent can be found in Appendix B.

3.3 Screening

All potential participants underwent pre-screening to determine if they were eligible to participate in the study. Pre-screening took place on the first day of testing. If the participant passed the pre-screening then they were allowed to continue with the remaining portion of the test. Individuals who failed to meet the pre-screening criteria were told immediately and were thanked for their interest.

The pre-screening consisted of each participant completing an Otological Normality Questionnaire and a concussion history questionnaire. (Appendix C). The ten-item Otological Normality Questionnaire was used to ensure that the participant was in good auditory health, with no previous ear surgeries or exposure to loud music that would negatively affect the test. The concussion history questionnaire was completed after the auditory questionnaire. Participants reported their previous medically diagnosed and self-perceived concussions. Participants in the test-retest reliability study were required to have less than 4 concussions in their lifetime and no injury or symptoms within the last 12 months. Participants in the athlete comparison cohort stage of the study were required to be symptom free within the last 6 months for their testing to be considered a baseline measures.

3.4 Heart Rate Variability

Heart rate variability measurements were based on standard resting HRV protocols from Berntson et al, 1997. Measurements were taken using the Polar Team2 Pro heart rate monitoring system (V1.3.04, California). Heart rate monitor straps (Team2 SoftStrap) were prepared for each participant by moistening the plastic electrodes on the reverse side of the strap, and attaching the individual wireless connector (Polar Team2 transmitter) to the strap. The strap was placed around the chest, directly on the skin, below the pectoral muscles approximately below the 10th rib. Once the monitor was connected to the tracking system (Polar Team 2 PC software) participants sat in a reclining chair that was reclined from 90 degrees to 180 degrees, to place the participants were in a supine position. The participants remained in the supine position for 10 minutes.

3.4.1 Heart Rate Variability Measurements

All HRV measurement was collected using the Polar Team2 pro software and sub evaluated using the Kubios (V2.2) University of Eastern Finland heart rate variability analysis software. Five minute supine samples of R-R intervals were analyzed using the *very low artefact correction factor* provided by the Kubios software. Seven frequency domain variables and three time domain variables were used to assess the different measurements that can be derived from HRV assessment. Each measurement and its description can be found in Table 3.1. Frequency domain variables represent the outcome of the spectral analysis of the R-R intervals within five minute supine sample using a fast

Fourier Finite Transform application (Kubios, Finland) and Welch's periodogram: 256 s window with 50% overlap. Time domain methods used standard arithmetic computations and were applied directly to the same five-minute resting sample (Tarvainen et al., 2013).

Table 3.1.Description of HRV variables and normative scores based on research.

Variable	Definition	Task Force, 1996	Nunan, Sandercock & Brodie, 2010		Zhang, 2007
			Male	Female	Age 20+ N=63
LF (ms^2) low frequency	Power in the range of 0.04-0.15Hz. Indicator of sympathetic drive	1170 ±416	356	414	346.8 ± 305.0
HF (ms^2) high frequency	Power in the range of 0.15-0.4HZ. Indicator or Vagal and parasympathetic drive	975 ± 203	475	516	216 ± 300.3
LF/HF	Ratio of low frequency to high frequency	1.5-2.0	2.3	1.2	2.78 ±2.3
Total Power (ms^2)	Variance of all of the NN intervals less than 0.4hZ	3466 ± 1018			872 .5 ± 695.1
LFnorm (n.u.)	Low frequency power expressed in normalized units LF/(total power-VLF) x 1000	54 ± 4	53	46	65.0 ±17.3

HFnorm (n.u.)	High Frequency power expressed in normalized units HF/(total power-VLF) x100	29 ± 3	39	38	34 ±17.4
RMSSD (ms)	Root mean square of the standard deviation of the difference between NN intervals	27 ±12	21	19	43.8 ± 26.8
pNN50	The number of pairs of adjacent NN intervals differing by more than 50ms (NN50) divided by the total number of all NN intervals	-	-	-	--
Mean HR	The average heart rate over a 5 minute period	-	-	-	-
Mean R-R interval (ms)	The mean of all R-R intervals in a five minute sample	-	922	885	761.0 ± 132.3

3.4.2 Heart Rate Variability Data Analysis

For spectral analysis of HRV, R-R intervals from the five-minute resting sample were exported from Polar to Kubios Heart Rate variability Software (V 2.2) in beat-to-beat format. Samples were subjected to the *very low-level artefact correction*, to reduce noise and errors from the Polar sample. A five-minute resting sample was selected for analysis. Selection of the sample was at the researcher's discretion, but started 3 minutes

into the recording to ensure that the participants were at true resting HRV and lasted 5 minutes in total.

3.5 Contralateral Auditory Suppression of Transient Evoked Oto-Acoustic Emissions

Assessing CAS TEOAE requires a multi-step process. Participants are first required to complete the Ontological Normality Questionnaire and an otoscopy to ensure there were no abnormalities in the ear and ear canal prior to testing. Complete CAS TEOAE testing was carried out using the test paradigm and protocol of Otodynamics ILO 292 V6 otoacoustic emission analyzer (London, UK). The first step measured the transient evoked otoacoustic emission (TEOAE) in each ear, for each participant. This test was performed in the right and left ear. UGD TE+DPOAE probes (Otodynamics Audiology Systems, A80-16-10) were fitted into the participant's ears at the beginning of testing, and remained in place until testing was completed. The TEOAE was measured in the test ear at a peak equivalent sound pressure (pe SPL) of 80 dB. A click presentation rate using 50 clicks per second using a linear technique (continuously). After TEOAE was measured and the response demonstrated a parameter estimate of >70% stability and reproducibility, the participant moved onto the spontaneous OAE (SOAE) test. The SOAE has no direct clinical application, but it is important in interpreting TEOAE and CAS TEOAE (Killan, Lutman, Thyer & Montelpare, 2012). The SOAE was measured in a manner known as synchronized SOAE (SSOAE) that are long lasting oscillations (Bright, 2002) again in right and left at 80 dB pe SPL in a non-linear, spontaneous

method at 50 licks per second. The presence of SOAEs was recorded if the response had amplitude greater than -25 dB SPL (Killan, Lutman, Thyer & Montelpare, 2012). The final step in CAS TEOAE testing was the estimate of contralateral auditory suppression. This method of testing operates two separate OAE recordings, one when a suppressor is present in the opposite (contralateral) ear and one without the suppressor present (ipsilateral) ear. The recording of the two tests is switched every three seconds to minimize the effect of changes in the ear. For this test the TEOAE level was set at 60 dB pe SPL linear click, and the suppressor or masker level is set at 65 dB pe SPL broadband noise (BBN) consistent with the test parameters recommended by Hood et al. (1995) to maximize the suppressive effect, while not evoking the auditory reflex and giving false results. Quantification of suppression was estimated using a customized computer code and can be found at: http://health.ahs.upei.ca/concussion/CASfrm3.php. (Montelpare, 2014). One main problem with testing contralateral suppression, in that when switched from assessing the right ear to the left ear, there is no way to ensure that the probe is getting an adequate signal for broadband noise. This problem was mediated by doing a check fit for both left and right ear at the beginning of the assessment, and instead of switching the probes in the participant's ears, the probe sockets were switched in the device. All data were stored on a secure server at UPEI. All parameters for the suppression test can be found in Figure 3.1. Total test time for all of the steps was approximately 12 minutes. All otological testing was carried out in conjunction with HRV analysis and therefore measured while the participant was in the supine position

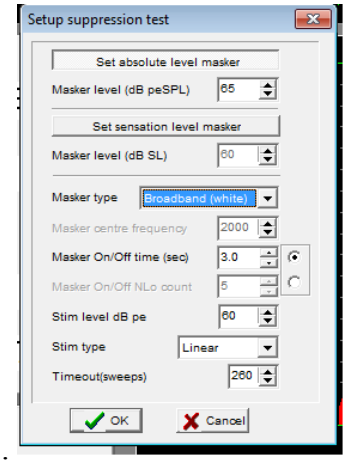

Figure 3.1 Parameters for the test set up for CAS TEOAE using the Otodynamics Audiology system

3.5.1 CAS TEOAE Measurements

CAS TEOAE was measured using four different variables and two different frequencies of measurement. The frequencies of 1414Hz and 2000Hz were chosen as they demonstrated the highest confidence levels and were supported by the literature in having consistently the highest confidence levels and best suppression values. Description of the four variables can be found in Table 3.2 below. The scores for the right (x) and left (y) ipsilateral ears for suppression were determined by calculating the difference between the TEOAE click at 60 dB and the BBN at 60 dB assessed in the ipsilateral ear. Sum scores were calculated by adding the measurement values recorded for the right and left ears and the difference scores (Diff) were calculated by subtracting the measurement values for the right and left ears. Thus the suppression score for the right ear at 1414Hz is X1414 and so on.

Table 3.2 Description of the variables for CAS TEOAE

R (dB)	The difference in dB of the sums of sounds recorded in the ipsilateral (right) l ear when just the click stimulus is present, and then the contralateral white broadband noise is present. (On 3 seconds, off 3 seconds)
L (dB)	The difference in dB of the sums of sounds recorded in the ipsilateral (left) ear when just the click stimulus is present, and then the contralateral white broadband noise is present. (On 3 seconds, off 3 seconds)
Sum =R+L (dB)	Sum of the suppression values in the right and left ear, i.e. total suppression
Diff =$\|\boldsymbol{R}-\boldsymbol{L}\|$ (dB)	Absolute value of the difference in suppression of the right and left ear.

3.6 Depression, Anxiety and Stress Scale (DASS-21)

The DASS-21 (Lovibond & Lovibond, 1995) was administered as an online survey. The 21-item survey was administered with a drop down menu after each question with the four response options. Once the survey was completed it was submitted to an online database along with a unique ID number for each participant. The survey can be analyzed as a whole or it can be broken down into three different subscales, depression, anxiety and stress. Each subscale has 7 specific questions. The complete survey can be found in Appendix D

3.7 Pain Anxiety Symptom Scale (PASS-20)

The PASS-20 (McCracken and Dhingra, 2002) was also administered online.. The 20-item survey was scored using a 5-point ordinal scale with responses ranging from 0-5 with 0 meaning “never” and 5 meaning “always”. Once the survey was completed the data were stored in a secure database. Information could only be identified by an assigned ID number that was only available to the research team. The complete survey can be found in Appendix E.

3.8 Phase one- Test Retest Stability

Phase one of this study used a test-retest design study was to evaluate the stability of HRV and of CAS TEOAE in a healthy young adult population (n=25). The complete demographic information for these participants can be found in Table 3.3. Participants were recruited via word of mouth and social media recruitment. Participants were asked to come to two different testing sessions, separated by a two-week period. Before each session they were asked not to wear headphones with music, to have clean ears and abstain from coffee or energy drinks for 12 hours prior to testing. Once participants were cleared through the pre-screening protocol (as described above) they underwent testing for both HRV and CAS TEOAE simultaneously.

3.8.1 Statistical Analysis

Data the first phase test-retest reliability was analyzed using a nonparametric statistical analysis technique, because the HRV data were nonparametric. CAS TEOAE was analyzed in the same manner for consistency in the analysis. The McNemar Chi-Square Statistic (1) and the Kappa z-score of agreement (2) were used to establish the test retest reliability of HRV and CAS TEOAE. The data were analyzed using a custom design webulator located at: http://health.ahs.upei.ca/webulators/mcnkap2.php and the code for this webulator is in Appendix F. (Montelpare & McPherson, 2000). Coefficient of variation and a paired t-test were also calculated to assess variation in the sample to account for the CAS TEOAE data being parametric.

(1). McNemar= $\sqrt{\frac{(|a-b|-1)^2}{(a+b)}}$

(2) Kappa 1.Compute row percentages

row 1= p1.=(a+b)/N

row 2= p2.=(c+d)/N

column 1= p.1=(a+c)/N

column 2= p.2.=(b+d)/N

2. Compute pi terms

O_{obs}=(Cell a)+(Cell d)

O_{exp}= (p1.*p.1) +(p2.*p.2)

3. Compute Kappa

Kappa= $\frac{(Oobs-Oexp)}{(1-Oexp)}$

(3) Coefficient of Variation=Standard Deviation /Mean

Table 3.3. Demographics of participants for Phase 1 and Phase 2

	Phase 1	Phase 2
Participants (n)	25	75
Male (n)	9	23
Female (n)	16	52
Height (cm)	171.6 ± 7.3	168.6 ± 9.6
Weight (kg)	71.2 ±2.9	152.6 ± 25.2
Previous concussion	0	23
Sport	-	Basketball- 7 Hockey-18 Soccer- 29 Rugby- 8 Swimming- 4 Field Hockey- 9

A paired t test was also used to evaluate the statistically difference between day one and day two. The webulator used for that assessment can be found at: http://health.ahs.upei.ca/webulators/t2smplpool2.php (Montelpare, 2015)

3.9 Phase Two- Athlete Baseline Testing

A convenience sample of UPEI varsity athletes (n=75) from six different sports: (i) soccer, (ii) rugby, (iii) field hockey, (iv) basketball, (v) hockey and (vi) swimming, were asked to participate in baseline screening. Participants were recruited via a third party email, and registered for appointments. Descriptive participant statistics for this cohort can be found in Table 3.1. During various pre-season training camps in September 2014 athletes were asked to complete the DASS-21 and PASS-20, as well as an online consent form prior to arriving the clinic for testing. Once the surveys were completed, participants scheduled appointments at the UPEI Concussion Evaluation Clinic. At the clinic, participants were evaluated on the CAS TEOAE and HRV simultaneously (as above). Testing was done simultaneously for the sake of time, as participants were doing other neurocognitive and concussion screening tests during this appointment.

3.9.1 Statistical Analysis

Univariate statistics were used to demonstrate the overall measures of central tendency and variance for the measures selected in this cohort. A set of measurements was selected for each of the objective tests. For example, while HRV used 11 measurements, the following five were used to represents the entire set of measurements:

(i) LF, (ii) HF, (iii) LF/HF, (iv) RMSSD and (v) mean HR. Similar to the establishment of a representative sample in HRV testing, the CAS TEOAE included 8 measurements. These measurements were selected as they showed the highest stability in phase one, were not a redundant measurement, were consistently used in the literature and were the most consistent in the athletes baseline testing. A total of 4 measures were selected from the original set to represent all measurement of the CAS procedure :(i) Y1414, (ii) Sum1414, (iii) X2000, (iv) Diff2000. Theses measurements were selected as they showed the highest confidence levels in the athlete baseline testing and evaluated all four of the different aspects of CAS TEOAE.

Further, because the participants were drawn from the larger sample of varsity athletes enrolled at UPEI, tests for homogeneity of variance using the coefficient of variation was used to enable the researcher to quantify the variance within each sample. A univariate multiple regression approach was used to quantify relationships between the measures for the DASS-21 and the PASS-20 independently with the following set of predictor variables: CAS TEOAE, demographics, activity type, and concussion history in one stage. The measures for the DASS and the PASS were analyzed independently with measures of HRV, demographics, activity type, and concussion history in a second stage.

The relationship between CAS TEOAE and HRV with the subscales of the DASS-21 and PASS-20 were evaluated using the Spearman Correlation Coefficient tested the relationships with CAS TEOAE and HRV and the subscales. The DASS-21 and PASS-20 subscales were created by separating the responses of the DASS-21 and

PASS-20 independently, into two groups: individuals that scored above the fiftieth percentile and individuals who scored below the fiftieth percentile on the psychological scales. Next, the Spearman Correlation Coefficient test was used to assess the two groups independently for the DASS-21 and PASS-20 subscales, as well as to determine if there was a significant relationship between the selected measures of the HRV test and the CAS TEOAE test. Finally, logistic regression analysis was used to evaluate the relationship between the DASS-21 and PASS-20, independently by concussion history for the given measurements of HRV and the CAS TEOAE test. The SAS program that was used for the Spearman Correlation Coefficient and Logistic Regression can be found in Appendix G

3.10 Phase Three- Case Study

Throughout the testing period varsity athletes were told to present themselves to the clinic if they suffered a concussion or presented with concussion symptoms at any time during the season. It was observed that during the 2014-2015 season, four varsity athletes contacted the Concussion Evaluation Clinic with injuries related to participation in sporting events. Of the four athletes reporting concussion, two had completed the baseline testing completely, and one consented to have the post-injury evaluation completed. This latter participant presented to the clinic two days post injury, and completed four assessments of HRV and CAS TEOAE. Data from the Sum1414 variable in CAS TEOAE and the LF/HF ratio in HRV are presented here to demonstrate the

dynamics of the recovery process with regard to the original injury recovery process curve presented in Appendix A.

Chapter 4

Results

4.1 Phase One Results

The mean scores and standard deviations were calculated for all eleven variables of HRV and eight variables of CAS TEOAE. Table 4.1 shows all HRV variables and Table 4.2 shows all CAS TEOAE variables and a two-tailed t-test. As a first test of stability, the pair wise t-test was computed for each of the variables in both HRV and CAS TEOAE measures independently. Based on the decision rule of - $t_{critical}$-2.06 $p \geq 0.05$, degrees of freedom=24 no significant difference was observed between measures on day one versus measures on day two.

Table 4.1.Mean scores ± standard deviation and t-test value for the test retest reliability for all HRV measurements (n=25).

	Day 1	Day 2	t-test
LF (ms2)	2534.81 ± 2078.7	1706.38 ± 1514.3	1.61
HF (ms2)	3932.52 ± 4412.0	3806.97 ± 3805.2	0.11
LF/HF	1.18 ± 0.97	0.838 ± 0.44	1.36
Total Power	8057.20 ± 6969.80	8337.88 ± 7332.90	-0.14
RMSSD	87.4 ± 74.3	69.15 ± 36.1	1.10
pNN50 (%)	39.91 ± 25.20	36.93 ± 24.8	0.42
Heart Rate (bpm)	66.83 ± 9.41	66.21 ± 8.93	0.23
RR (ms)	926.43 ± 139.76	919.62 ± 126.87	0.18
SDNN (ms)	93.50 ± 57.76	88.14 ± 41.26	0.38
LF norm (n.u.)	42.80 ± 20.10	38.38 ± 20.92	0.76
HF norm (n.u.)	55.40 ± 20.34	59.36 ± 24.03	-0.64
df=24, $p<0.05$, $t_{critical}$-2.06 decision rule: $t_{observed} > t_{critical}$ then reject H_0 $x_1 \neq x_2$			

*Table 4.2.*Mean scores ± standard deviation and t-test value for the test retest reliability for all CAS TEOAE measurements (n=25).

	Day 1	Day 2	t-test
X1414	1.07 ± 1.96	0.52 ± 2.5	1.10
Y1414	1.08 ± 2.53	1.58 ± 1.58	-0.84
Sum1414	2.11 ± 3.39	2.12 ± 2.98	-0.01
Diff1414	1.98 ± 2.18	1.99 ± 2.15	-0.02
X2000	1.03 ± 1.33	0.79 ± 0.82	0.76
Y2000	0.64 ± 1.78	0.6 ± 0.96	0.10
Sum2000	1.60 ± 2.18	1.28 ± 1.4	0.62
Diff2000	1.32 ± 1.63	0.56 ± 0.96	2.01
df=24, $p<0.05$, $t_{critical}$-2.06 decision rule: $t_{observed} > t_{critical}$ then reject H_0 $x_1 \neq x_2$			

The next step in measuring the stability and the agreement between the objective measures of HRV and CAS TEOAE between test days was to use the McNemar test of symmetry, and the Kappa statistic for agreement. To calculate the McNemar test of symmetry a binary scale was used based on the median score for each variable on each test day. Each data point was assessed on the binary scale where 0 indicated a score below the median and 1 indicated a score above the median. Using the McNemar Chi Square, data points were assigned to a cell in a two by two table based on whether the individual scored the same on the binary scale for day one and day two. Figure 4.1 presents the structure of the McNemar Chi Square test to determine the probability that an individual will score the same on day one and day two.

	Test day 1		
Test Day 2		1	0
	1	**A**	**B**
	0	**C**	**D**

Figure 4.1. Diagram of the McNemar Chi Square

The results indicate that there were no significant differences between day one and day two for any of the variables of the objective measures of HRV and of CAS TEOAE. Table 4.3 shows the McNemar scores for HRV, and Table 4.4 shows the McNemar scores for CAS TEOAE.

Given that the variables were not statistically different between test days for the objective measure of HRV and CAS TEOAE, the Kappa statistic of agreement was used to assess whether there was significant agreement between the two test days. The Kappa statistic also uses the Chi Square, Figure 4.1, but assesses if the variables differ significantly from what is expected by chance. The z_{Kappa} is shown to be significant if the kappa score is significantly different from zero and is falling outside the region of acceptance ($-1.96 \leq x \geq 1.96$). We can conclude that there is significant agreement between day one and day two. Three variables showed significant agreement for the objective measures of HRV and CAS TEOAE: RMSSD ($z=2.22$) and Mean HR ($z=2.65$), and Sum1414 ($z=2.2$)

*Table 4.3.*Test retest data for interclass correlation, McNemar statistic and Kappa z score for HRV measurements.

	McNemar	95% CI Kappa	Kappa Score	z_{kappa}
LF/HF	-0.3	0.018-0.225	0.124*	0.61
LF	0.3	0.009-0.222	0.582*	0.12
HF	0.63	0.104-0.283	0.981*	0.19
RMSSD	0.38	0.362-0.52	0.441*	2.22*
HR	-0.822	0.431-0.631	0.522*	2.65*
Total Power	1.26	0.139-0.299	0.219	1.15
PNN50	-0.3	0.017-0.266	0.121	0.61
RR	-0.71	0.29-0.44	0.363	1.84
SDNN	0	0.11-0.29	0.2	0.99
LF n.u.	0	0.28-0.43	0.351	1.75
HF n.u.	-0.3	0.017-0.23	0.121	0.61

* denotes a significant result

*Table 4.4.*Test retest data for the McNemar statistic and Kappa z score for CAS TEOAE measurements.

	McNemar	95%CI Kappa	Kappa Score	Z_{kappa}
X 1414	0.24	0--0.117	-0.357	-1.79
Y1414	0.33	0.199-0.354	0.277*	1.39
Sum1414	-0.38	0.359-0.516	0.437*	2.2*
Diff1414	-0.58	0-0.167	0.045	0.23
X2000	-0.71	0.282-0.482	0.3548*	1.8
Y2000	-1.81	0--0.025	-0.229	-1.4
Sum2000	1.6	0-0.06	-0.206	-1.21
Diff200	-1.67	0.235-0.372	0.303*	1.65
* denotes a significant result				

4.2 Phase Two Results

The mean scores for the objective measures of HRV and CAS TOAE in a sample of 75 athletes were compared to the Day 1 mean scores for the cohort of individuals used in establishing the stability of the HRV and CAS TEOAE tests. The mean scores for all variables of the objective measures of HRV and CAS TEOAE were not statistically different based on the confidence interval comparison where $t_{critical}$-1.99 p-value≤0.05 and degrees of freedom= 98.

Since the variables were not statistically different from the test retest population, the range of variation in scores for the 75 athletes was tested for variability using the

coefficient of variation. Table 4.5 shows the variables used for phase 2, their mean scores, coefficient of variation and t-test values for HRV and Table 4.6 shows the variables for CAS TEOAE their mean scores, coefficient of variation and t-test values.

Table 4.5.The mean scores, coefficient of variation and pair t-test values for variables of HRV for n=75 varsity athletes.

	Mean	StD	CV	t-test
LF	4278.94	15014.56	3.51	0.98
HF	4648.63	7565.97	1.63	0.58
LF/HF	0.82	0.62	0.76	-1.74
RMSSD	102.83	71.35	0.69	0.91
HR	64.19	9.74	0.15	-1.19
df=98, $p<0.05$, $t_{critical}$-1.99 decision rule: $t_{observed} > t_{critical}$ then reject H_0 $x_1 \neq x_2$				

*Table 4.6.*The mean scores, coefficient of variation and pair t-test values for variables of CAS TOAE for n=75 varsity athletes.

	Mean	StD	CV	t-test
Y1414	1.06	1.98	1.87	-0.036
Sum1414	2.52	4.21	1.67	0.49
X2000	1.09	1.61	1.47	-1.08
Diff200	1.43	2.24	1.54	0.27
df=98, $p<0.05$, $t_{critical}$-1.99 decision rule: $t_{observed} > t_{critical}$ then reject H_0 $x_1 \neq x_2$				

The baseline scores of the subscales of the DASS-21 (Table 4.7) and PASS-20 (Table 4.8) were assessed for significant relationships between the selected variables of the objective measures of HRV and CAS TEOAE.

*Table 4.7.*Mean scores for the DASS-21 subscales at baseline testing of 75 UPEI varsity athletes

DASS-21	Mean	StD
Depression	1.44	2.73
Anxiety	2.51	2.87
Stress	2.59	3.29

*Table 4.8.*Mean scores for the PASS-20 subscales at baseline testing of 75 UPEI varsity athletes

PASS-20 subscales	Mean	StD
Escape	5.67	4.02
Fear	3.83	3.94
Cognitive	8.04	4.7
Physiological	3.03	3.59

Given that there were no significant correlations between the subscales of the DASS-21 or the PASS-20 with the objective measures of HRV and CAS TEOAE, the next step was to create binary groups for the subscale scores of the DASS-21 and the PASS-20. In this process, each individual subscale score was separated into two groups

by splitting the scale at the median score. Table 4.9 reports the subscale median scores and the subsequent number of individuals in each binary group.

Table 4.9.Distribution of number of participants based on responders and non-responders for the subscales of the DASS-21 and PASS-20, where group 0 is non-responders, and group 1 is responders.

	Group 0	Group 1
Anxiety Group Median = 2	n=33	n=42
Depression Group Median= 0	n=43	n=32
Stress Group Median= 1	n=28	n=47
Fear Group Median= 5	n=34	n=41
Cognitive Group Median = 7	n=32	n=43
Escape Group Median =5	n=41	n=34
Physiological Group Median = 2	n=44	n=31

The DASS-21 and PASS-20 subscale group scores were used as the dependent variables, first in Spearman correlations with the objective measures of HRV and of CAS TEOAE, and second as dependent measures in logistic regression models intended to determine the influence of objective measures of HRV and of CAS TEOAE on subscale reports of the DASS-21 and PASS-20.

The results indicated that there was a significant relationship found in the escape/avoidance group of the subscale of the PASS-20 and the LF/HF ratio measurement of HRV ($p< 0.05$, $r_{sp}=-0.25$). There were no other significant relationships

found between the other subscales of the PASS-20 and the subscales of the DASS-21 and the objective measures of HRV. Similarly there were no significant pairwise correlations observed between the subscale group scores for the DASS-21 and PASS-20 with the objective measures of CAS TEOAE.

In the next phase of statistical analysis, logistic regression was used to determine the influence of the objective measures of HRV and of CAS TEOAE on the independent subscale groups of the DASS-21 and PASS-20. The results indicate that the escape/avoidance subscale group was predicted by LF/HF and mean heart rate (Table 4.10), the cognitive group was predicted by LF/HF and mean heart rate (Table 4.11), the stress group was predicted by mean heart rate and RMSSD (Table 4.12), the fear group was predicted by LF/HF and mean heart rate (Table 4.13), the anxiety group was predicted by mean heart rate and RMSSD (table 4.14) and the physiological group was predicted by LF/HF (Table 4.15).

Table 4.10.Analysis of Maximum Likelihood Estimates (dependent variable= Escape Group; r square= 0.18)

Predictor Variables	Parameter Estimate	Standard Error	Wald Chi-Square	p value
LF/HF	-1.35	0.55	6.002	0.014
Mean HR	0.021	0.010	4.16	0.041

Table 4.11.Analysis of Maximum Likelihood Estimates (dependent variable= Cognitive Group; r square= 0.106)

Predictor Variables	Parameter Estimate	Standard Error	Wald Chi-Square	p value
LF/HF	-0.84	0.47	3.19	0.074
Mean HR	-0.019	-0.010	3.62	0.057

Table 4.12.Analysis of Maximum Likelihood Estimates (dependent variable= Stress Group; r square=0.13)

Predictor Variables	Parameter Estimate	Standard Error	Wald Chi-Square	p value
Mean HR	0.026	0.011	6.14	0.013
RMSSD	-0.011	0.0063	3.22	0.073

Table 4.13.Analysis of Maximum Likelihood Estimates (dependent variable= Fear Group; r square= 0.091)

Predictor Variables	Parameter Estimate	Standard Error	Wald Chi-Square	p value
LF/HF	-0.88	0.47	3.57	0.059
Mean HR	0.02	0.0099	3.98	0.046

Table 4.14.Analysis of Maximum Likelihood Estimates (dependent variable= Anxiety Group; r square= 0.12)

Predictor Variables	Parameter Estimate	Standard Error	Wald Chi-Square	p value
Mean HR	0.022	0.011	4.12	0.032
RMSSD	-0.014	0.0070	3.87	0.049

Table 4.15.Analysis of Maximum Likelihood Estimates (dependent variable= Physiological Group; r square= 0.12)

Predictor Variables	Parameter Estimate	Standard Error	Wald Chi-Square	p value
LF/HF	-1.03	0.58	3.18	0.075

As a result of identifying these significant objective predictors of the anxiety subscale group of the DASS-21 and the fear subscale group, cognitive subscale group and escape/avoidance subscale group of the PASS-20 a subsequent logistic regression analysis was used to determine if these relationships were present when the data were separated according to concussion history. Table 4.16 shows the distribution of participants based on concussion history and gender. However, the data were not separated by gender in subsequent analyses because of the smaller cell size.

Table 4.16. Distribution of participants by sex and presence of concussion history for a sample of n=75 varsity athletes.

	Male	Female
No concussion history	17	31
Yes concussion history	6	21

The results indicated that in the sub classification of individuals with no previous concussion history demonstrated the same findings as the total group. That is, the escape/avoidance group was predicted by LF/HF and mean heart rate (Table 4.17), stress group was predicted by mean heart rate (Table 4.19), fear group was predicted by LF/HF

and mean heart rate (Table 4.20) and anxiety group was predicted by mean heart rate and RMSSD (Table 4.20). However, the similarities in relationships were not present in the group that reported a previous concussion. The depression group was predicted by mean heart rate (Table 4.18), which was not present in the total group, or the group with no previous concussion. In particular where the LF/HF ratio was a significant predictor of the escape/avoidance subscale group in the concussed group, this significant finding was not observed in the group of individuals that had reported a previous history of concussion.

Table 4.17.Analysis of Maximum Likelihood Estimates for no previous concussion history (dependent variable= Escape Group r square= 0.26)

Predictor Variables	Parameter Estimate	Standard Error	Wald Chi-Square	p value
LF/HF	-1.79	0.80	4.96	0.026
Mean HR	-0.039	0.015	6.81	0.0090

*Table 4.18.*Analysis of Maximum Likelihood Estimates for yes to previous concussion history (dependent variable= Depression Group r square= 0.17)

Predictor Variables	Parameter Estimate	Standard Error	Wald Chi-Square	p value
Mean HR	-0.043	0.026	2.78	0.095

*Table 4.19.*Analysis of Maximum Likelihood Estimates for no previous concussion history (dependent variable= Stress Group r square= 0.17)

Predictor Variables	Parameter Estimate	Standard Error	Wald Chi-Square	p value
Mean HR	0.026	0.013	4.35	0.037

Table 4.20.Analysis of Maximum Likelihood Estimates for no previous concussion history (dependent variable= Fear Group r square= 0.20)

Predictor Variables	Parameter Estimate	Standard Error	Wald Chi-Square	p value
LF/HF	-1.60	0.81	3.91	0.048
Mean HR	0.028	0.014	4.12	0.043

Table 4.21.Analysis of Maximum Likelihood Estimates for no previous concussion history (dependent variable= Anxiety Group r square= 0.25)

Predictor Variables	Parameter Estimate	Standard Error	Wald Chi-Square	p value
Mean HR	0.035	0.014	5.99	0.014
RMSSD	-0.017	0.0093	3.25	0.071

In summary it was found that selected variables for the measurement of HRV and CAS TEOAE were stable between testing day 1 and day 2. There were no significant relationships between the object measures of HRV and CAS TEOAE with the psychological measures of DASS-21 and PASS-20. However, when the DASS-21 and PASS-20 subscales were broken down into two distinct groups of responders and non-responders and significant relationship was found with the escape/avoidance subscales of the PASS-20 and the LF/HF ratio. Upeon further breakdown of the group scores based on history of previous concussion, it was found that the group with no history of pervious concussion exhibited the same relationships with the DASS-21 and PASS-20 subscales as

the total population, but the group with a previous concussion history did not show those relationships, in fact they displayed the complete opposite relationships.

Chapter 5

Case Study

One varsity athlete presented to the Concussion Evaluation Clinic in January 2015 with a physician-diagnosed concussion. This participant had completed the full baseline profile in September 2014. During baseline testing the participant reported no previous history of concussion, and no general concussion symptoms based on the SCAT 3 symptom reporting section. The participant presented at the clinic 48 hours post injury, where the circumstances of the injury were recorded, symptoms were reported based on the SCATIII and the participant was assessed on the objective measures of HRV and CAS TEOAE. Following the injury, the participant was assessed four times: 1) 48 hours post injury, 2) 4 days post injury, 3) 7 days post injury and 4) 10 days post injury. The results of the athlete's symptom reporting (Figure 5.1) showed a decline over the course of the four days of testing, which is consistent with an expected recovery pattern.

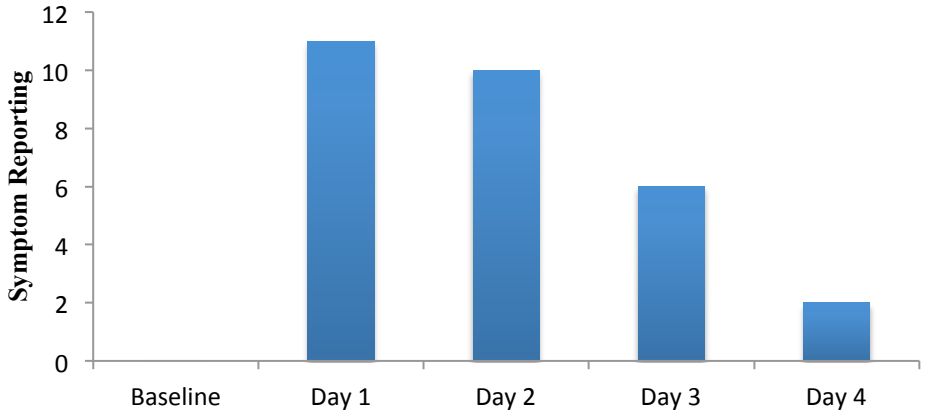

Figure 5.1 The baseline and post injury values for reported symptoms based on the symtpom reporting scale from the SCAT 3

For the objective measure of HRV and CAS TEOAE, one variable for each measurement was selected to assess the changes post injury and the subsequent recovery to baseline. The LF/HF ratio was selected as the objective measure of HRV, because it is an indicator of the sympathovagal balance and showed good stability in measures of test-retest reliability. The sum1414 measurement was selected as the objective measure to represent the CAS TEOAE test as it had the highest confidence interval over the four testing days for the participant and showed good stability in the measures of test-retest reliability. The post injury scores were again plotted with the baseline estimate to show the recovery of the athlete following injury. Figure 5.2 and Figure 5.3 show the two variables selected at baseline and the four days following injury for the objective measures of HRV and CAS TEOAE.

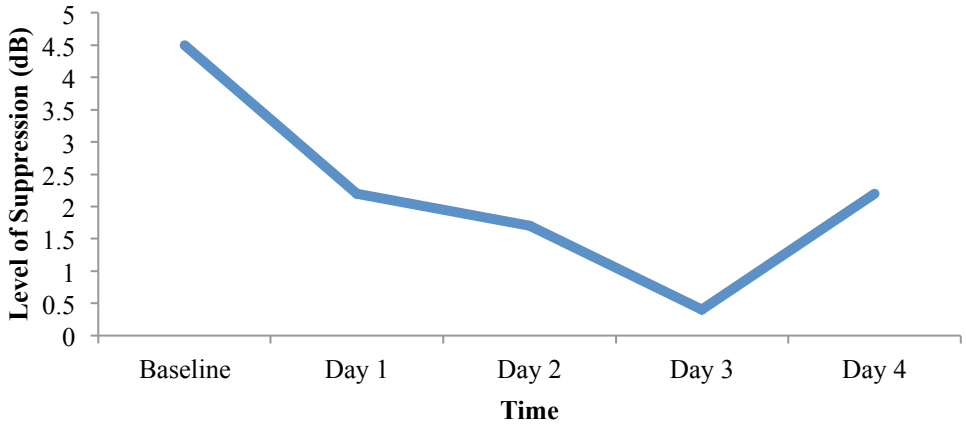

Figure 5.2 The baseline and post injury scores for sum1414 of the objective measure of CAS TEOAE for a concussed individual

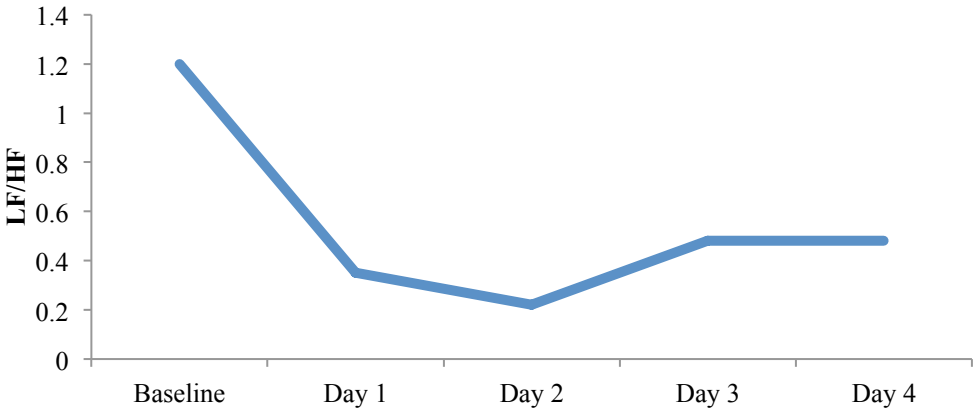

Figure 5.3 The baseline and post injury values for the LF/HF variable of the objective measure of HRV for a concussed individual

These figures were compared to the injury recovery hypothesis (Appendix A) to assess the return to a "healthy" baseline value. The participant demonstrated a 49% drop in the value of LF/HF and a 29% drop in the value of sum1414 post injury shown in Table 5.1. This drop in score indicates a change in HRV and decrease in suppression values for CAS TEOAE, followed by a steady increase towards the baseline value for each variable.

Table 5.1. Percentage change in the variables LF/HF and Sum1414 for the objective measures of HRV and CAS TEOAE following a concussion, compared to baseline values.

	Baseline	Day 1	Day 2	Day 3	Day 4	
Sum1414	100%	49%	38%	9%	49%	
LF/HF	100%	29%	18%	40%	40%	**RTP**

RTP: denotes return to play without subsequent follow-up

Chapter 6

Discussion

The primary purpose of this thesis was to assess the stability of HRV and CAS TEOAE as objective measures of concussion baseline assessments and return to play criteria. The results from phase one of the study, to determine measures of stability showed that the selected tests were stable from day one to day fourteen. Consistent with the findings from Fagard, Pardaens & Staessen (1999) there was large interindividual variability in the short term (measurement five minute sample) of HRV as indicated by large standard deviations between subjects. The large inter subject variability that was expected because of the observed physical variability across athlete groups. In this study athletes were homogenous, in that they were all identified as varsity level athletes, however the population consisted of athletes from six different sports, some of which are based on contact and other based on speed and agility, it was not surprising to observe high variability in this physiological measure given the physiological/ physical demands of the athletes in their respective sports. The large inter subject variance was an important consideration when using HRV as an indicator of physiological consequences of concussion. In other words, it was impossible to establish a definite starting point quantitatively to represent all athletes within the cohort. As a result, the nonparametric McNemar chi-square was used to provide an estimate of the stability of individuals on the selected measures on day one to day two. Likewise the Kappa statistic proved to be a valuable indicator of the measures of agreement between test measurements on each of

the evaluation days. The results of this process enable us to suggest that the specific measures from HRV (LF/HF and RMSSD) and the specific measures of CAS TEOAE (Sum1414 and Diff2000) may be considered as a stable and useful estimator of the physical consequence of a concussion. That is to suggest that these measures provide reliable estimates of baseline measures for two essential cranial nerve functions in an athlete population. Another important finding of this phase has been to build on the repeatability study of OAEs by Mishra & Lutman. Using a very comprehensive statistical analysis and perfect clinical settings Mishra and Lutman concluded that in normal hearing individuals the inhibition from contralateral suppression ranged from 0.96 dB to 1.47dB, which are similar to the mean scores calculated in phase one (2013). It is also important to note that phase one demonstrated the stability of CAS TEOAE in a non-clinical, less controlled setting than that of Mishra & Lutman, and therefore CAS TEAOE can be repeated in less than ideal settings and obtain similar results.

The secondary purpose of this thesis was to establish relationships with the psychological measures of DASS-21 and PASS-20 for the objective measures of HRV and CAS TEOAE by determining the relationships between the objective measures of HRV and CAS TEOAE with the psychological subscales of the DASS-21 and the PASS-20. Consistent with our expectation that since the measures of CAS TEOAE should function independently of emotional drive or underlying psychological events, CAS TEOAE variables did not correlate strongly with the psychologically based scale estimates of DASS-21 and PASS-20, as determined with a non-parametric Spearman

Correlation test. The DASS-21 and PASS-20 subscales - when computed as binary scores- provide estimates of an individual's emotional state in relation to depression and anxiety, and therefore should not be directly influenced by the physical disruption of a concussion injury.

Conversely, since heart rate is functionally influenced by emotional state through sympathovagal control (Appelhans & Luecken, 2006; Appelhans & Leucken, 2008) it was expected that the DASS-21 and PASS-20 subscales- when computed as binary scores- would correlate with measures of HRV. This expectation suggests that the activity of the vagal nerve can be quantitatively related to the scoring of emotional state. While this relationship was not observed in a simple pairwise correlation, based on the Spearman non-parametric correlation test, it was observed in a more sophisticated modeling approach based on logistic regression. In the development of the logistic regression model, the subscale of PASS-21- escape/avoidance (defined as an individual's drive to avoid situations which are perceived to cause pain) (McCracken & Dhingra, 2002) when scored as a binary variable was negatively associated with the LF/HF ratio measure of HRV. This relationship is described as follows: when an individual scored low on escape/avoidance, below the median score the LF/HF ratio score was high. A low score on escape/avoidance is expected under normal conditions, as is the predominance of sympathetic modulation of heart rate. Conversely a high score on escape/avoidance under normal conditions requires a predominance of parasympathetic modulation to

control the sympathetic drive of fight or flight, which translates to a low score on the LF/HF ratio (Figure 6.1).

The LF/HF ratio, mean heart rate and RMSSD were the HRV variables that consistently showed relationships to the psychological measure of DASS-21 and PASS-21. It is important to note that these variables were all highly correlated with one another using the Spearman Correlation Coefficient for the varsity athlete population.

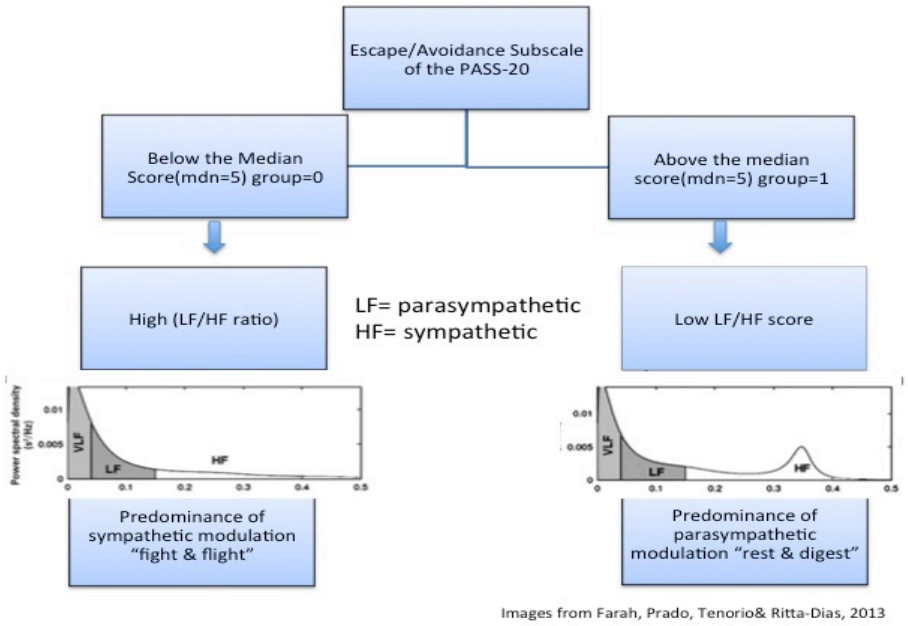

Figure 6.1 Description of the relationship of the escape/avoidance with the LF/HF ratio of HRV.

While this complex relationship was observed in the non-concussed cohort, no relationship between measures of HRV and DASS-21 or PASS-20 were observed in logistic regression analysis of the participants that reported a history of concussion.

Although this does not indicate a causal model, it does bring to light two different hypothesis as to why this occurred: one hypothesis is that individuals that reported a history of concussion respond differently than individuals that did not report a history of concussion on selected clinical tests. The second hypothesis is the sample of varsity level athletes was a majority of female and the literature tell us that females are more likely to report symptoms (Lovell et al, 2006) and are more likely to get concussed than their male counterparts in the same sport (Covassin, Swaink & Sachs, 2003)

6.1 Case Study

Underlying all of the research in establishing a baseline measure in concussion and decisions for return to play has been the injury-recovery hypothesis (Appendix A). In this particular study we were able to observe the dynamics of an individual moving from baseline levels, to post injury levels and returning close to baseline estimates over time (Figure 6.2). The post injury decline, followed by the subsequent increase was inversely proportional to the reported symptoms of the concussed individual. The results shown here indicate that in the injury recovery hypothesis exists and that an individual will demonstrate deficits in the objective measures of HRV and CAS TEOAE following a concussion injury with a subsequent return to or near baseline over a period of time. While this is exciting in itself, we were unable to show this in a larger cohort for a number of reasons: first, athletes typically both underreport and don't report injury (McCrea et al, 2004), they may not return to the clinic for post injury evaluation because it's not part of the typical post injury regimen. There is a need for further post injury

assessment to further support the return to play hypothesis. As we saw in both phase 1 and phase 2 of this study, there is high variability in the scores of HRV and in CAS TEOAE at baseline between individuals. It is important to have baseline estimates in order to properly assess the changes post injury as each individual case can have a different starting point. The significant difference in baseline scores could mean the different of a small decline post injury or a large one. Furthermore, concussion is associated with a stigma, especially in the athletic population, which leads to athletes self-diagnosing their recovery, and, in our case, choosing not to continue repeated testing once they were cleared to return to play.

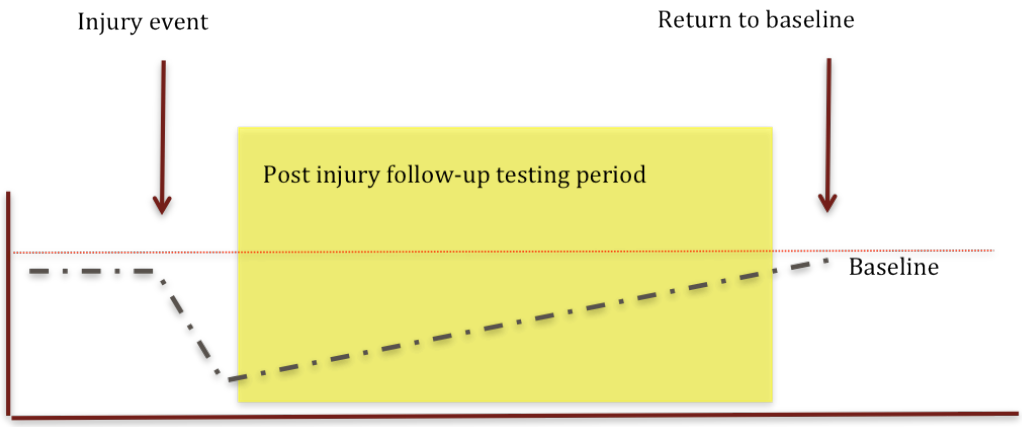

Figure 6.2The dynamics of the post-injury change in variables and return to baseline values over time (Montelpare, 2015)

6.2 Limitations

There were limitations identified in this research. Although sex did not emerge as a predictor for any of the subscales of the DASS-21 and PASS-20, there was a larger number of females (n=52) compared to males (n=23) that completed the surveys and

baselines testing. Lovell et al reported that healthy young females report more symptoms compared to healthy young males (2006) at baseline and post injury. McFadden, Martin, Stagner & Maloney reported a difference in TEOAE responses, but only at higher frequencies, therefore data was analyzed at lower frequencies (2009). It should also be noted that symptoms, health status and the DASS-21 and PASS-20 were measured outside the clinic and there has been a tendency for athletes to under report symptoms as noted in the research by McCrea et al (2004). There are also noted limitations to the measurement of CAS TEOAE. In conducting the CAS TEOAE measurement researchers typically use a soundproof room or booth where the computer system and tester are located external to the testing space. In the present study the testing was completed in close proximity to measurement equipment and a soundproof space was unavailable. Likewise, this testing may have been influenced by external noises associated with concurrent testing in other spaces in the clinic. All CAS TEOAE data ran 260 data sweeps, but some participants had a larger number of data point rejected because of external noise and test duration was longer. The attention to the CAS TEOAE linear click or broadband noise was not controlled. Research by De Boer & Thornton (2007) noted a change in suppression values based on whether participants were attentive to the sounds produced by the test or an arbitrary task. The effect of personal music devices was also controlled, using an otological questionnaire, based on self-report items may have been influenced by participant bias - with a possibility of underreporting. There are also some limitations for the measurement of HRV. The Polar Team2 Pro system and Kubios

Heart Rate Variability Analysis Software were used to evaluate the heart rate variability. These programs have been shown to provide reliable and stable estimates (Nunan et al, 2009), however the researchers noted differences in the number of artefacts present in the r-r wave samples.

There is also a statistical limitation as it pertains to the McNemar chi-square and the Kappa test of agreement. This approach was chosen as the HRV data was non-parametric and as such a non-parametric staticall approach was selected to best analyse the data. However, the CAS TEOAE data was analyzed in the same was, but the data is parametric, and was analysed the same in order to be consistent throughout the thesis.

6.3 Conclusions and Recommendations

In conclusion, the objective measures of HRV and CAS TEOAE are comprised of sub-scale estimates that were considered to be stable measures. When assessing psychological measures of the DASS-21 and PASS-20, outcomes on the subscales can be predicted by LF/HF, mean heart rate and RMSSD. These relationships are considered to be present within a cohort reporting a history of concussion. When history of previous concussion was considered in our analysis, significant relationships differed and therefore it is concluded that concussion injury may influence clinical outcomes. Based on the results from the case study it is recommended that the use of the objective measures of HRV and CAS TEOAE as baselines and post injury measurements for concussion be explored further. It is also recommended that the predictability of the PASS-21 by variables of HRV be explored further using a longitudinal research design. The outcome

of the case study demonstrated the need for further data collection for the analysis of the injury recovery hypothesis. It also points out the need for a concussion protocol to be implemented and that protocols and services be linked with the health care team to better assess the injury and return to play timelines.

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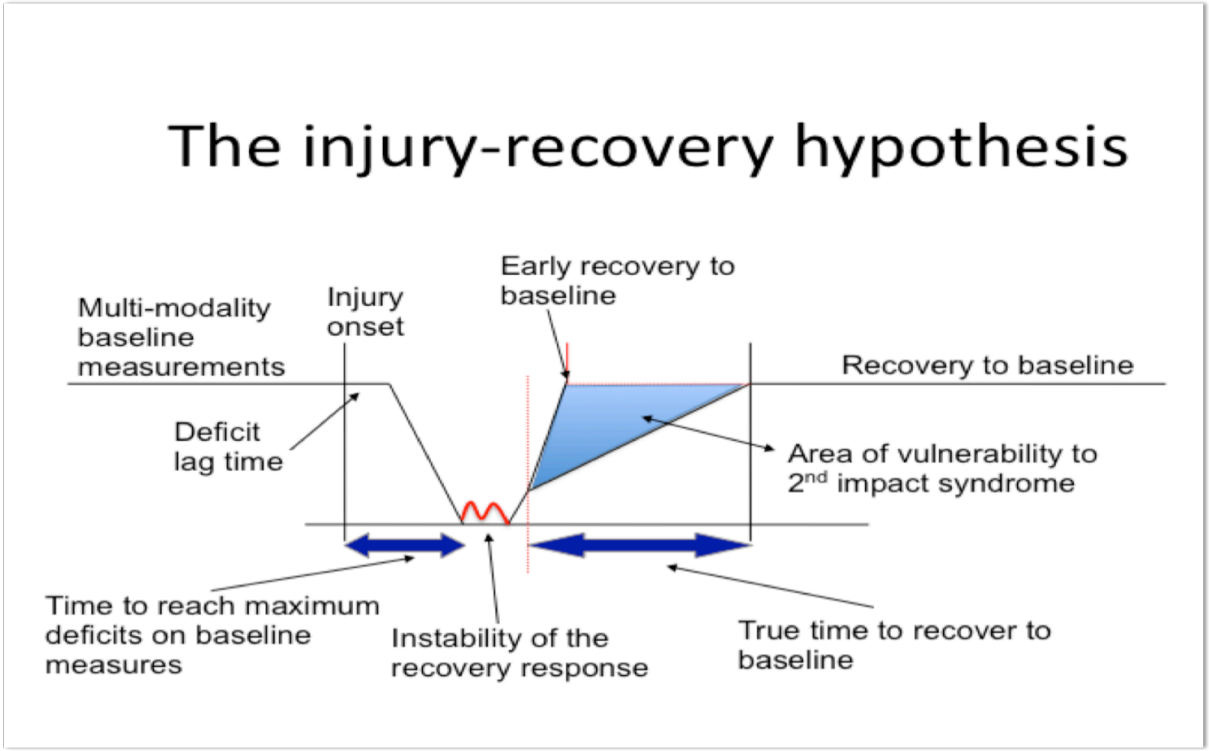
Appendix A

Injury Recovery Hypothesis



(Montelpare, et al., 2013)

The injury-recovery hypothesis following concussion injury.

Appendix B

Letter of Informed Consent

UPEI Concussion Evaluation Clinic

Establishing the test-retest stability of heart rate variability (HRV) and Contralateral Acoustic Suppression (CAS) in a sample of non-concussed college aged individuals

Scheduled Appointment Time:_____.

Please arrive **on-time** for your scheduled appointment. We are located in the lower floor of the Steel Building (Room 128).

Letter of Consent

At the University of Prince Edward Island (UPEI), we are conducting studies on how to best detect concussion and manage the recovery process for individuals that experience such an injury. Currently, there is no comprehensive single strategy for establishing return to play following a concussion injury, as there are inconsistencies across sport type and age group.

The purpose of our research is to examine the consistency for a series of non-invasive measures used to assess physical, and neurological function. We expect that the results of this work will contribute to decisions about an athlete's return-to-play following a concussion injury. "

Some basic guiding principles for the partnership between the researchers and the participants:

I have read the information sheet for this study and have been given permission to print any information I wish. I have also been provided a contact number of the Principal Investigator and an invitation to ask questions about the study or my participation in the study.

I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my legal rights being affected.

I understand that I will not benefit financially if this study leads to the development of education and training or future research/education/technological developmental outcomes.

I know how to contact the study team if necessary. I understand that I can contact the UPEI Research Ethics Board at (902) 620-5104, or by email at reb@upei.ca if I have any concerns about the ethical conduct of this study.

I understand that by submitting the letter of informed consent with this study I am agreeing to participate in this study.

I understand that a written summary of the findings will be available to participants through reports produced by the study team and disseminated via professional and academic journals and conferences.

Authorization

If you would like to participate in this research, please print this page and sign your name and date on the lines below. Please bring this form with you when you visit the UPEI Evaluation Clinic in the lower level of the Steel Building. This signed form is necessary for you to participate.

I have read the information provided for the research conducted at UPEI related to establishing baselines for concussion screening as described in the associated information page. My questions have been answered to my satisfaction and I agree to participate in this study. I voluntarily choose to participate in this study, but understand that my consent does not take away my legal rights in the case of negligence or other legal fault of anyone who is involved in this study. I have been given a signed copy of this consent form.

□ □By checking this box I am allowing any test results to be shared with UPEI healthcare professionals (ex. Physiotherapists or team doctors) or coaches

□By checking this box the participant indicates their interest of receiving study results at this email address _____

Name of Participant: _____

Signature:

Signature of parent if participant is under the age of 18

_____

DATE: _____

On the day of your appointment please keep in mind these points:

-The testing takes approximately **20 minutes**

-Sign and bring with you the attached "Letter of Consent"

-Avoid listening to loud music

If you have any questions or concerns please feel free to contact us at **concussion@upei.ca**

Thank you for your co-operation and participation!

Letter of Information

Background Information

Research about injuries sustained in sport and physical activities is not a new topic and despite the attention that various forms of media spotlight on catastrophic events in

sports, we still know very little about the true rate of injuries or effective strategies to reduce the risk of injury. A benefit of the recent attention to injury prevalence has been through the support of research into the causes, rates, and outcomes- both immediate and long term, to the effects of injury. As such, the purpose of this study is to use a prospective multiple cohort design to determine the most effective baseline testing and in-season screening with concomitant post-injury evaluation, for an athlete's readiness to return to activity following a traumatic brain injury (a concussion).

Purpose

The purpose of this study is to identify the statistical significance of Heart rate variability (HRV) and Contralateral acoustic suppression of transient evoked oto-acoustic emission (CAS TEOAE) as measurement of concussion.

What is expected if I decide to participate?

If you choose to participate we will ask you to sign a consent form. After that you will schedule an appointment at the UPEI concussion evaluation clinic (Steele Room 128).This study will have 25-30 participants, and take approximately 20 minutes per person to complete.

CAS TEOAE assessment

Participants will be seated, while a pair of small non-invasive probes similar to personal music system earphones will be placed in each ear canal (Otodynamics, UK) similar to personal music system earphones will be placed in each ear canal. CAS TEOAE measurements will be conducted following the default test paradigm employed by the Otodynamics ILO 292 otoacoustic emission analyzer (Otodynamics, UK). The test typically lasts approximately 2 minutes per ear and will not cause any harm to the participant. During TEOAE testing participants are asked to remain quiet and still. If any test results indicate the need for further audiological testing, participants will be given

appropriate advice and will have an opportunity to discuss any concerns with a registered audiologist.

HRV assessment

The proposed method for measuring heart rate variability (HRV) will be based on those previously published in related studies (Berntson, Bigger, Eckberg, Grossman, et al, 1997; Borella, Langbeinb, Desprésc, Hansen, et al, 2007). After the individual places the heart rate monitor strap across their chest, we will ask them to lie down on a standard reclining chair. After the individual has been resting in the supine position for 8 minutes we will be induce a response of the parasympathetic system by asking the person to stand from a lying position. This approach is considered to be consistent with the recommended method in which an individual is asked remain in a supine resting position to allow for spectral and temporal analysis, followed immediately by a HRV measurement upon standing, which alters autonomic nervous system balance. The HRV assessment will run simultaneously with the CAS TEOAE assessment. In total testing will take approximately 20 minutes in total.

There are no known risks or harm associated with this research.

Confidentiality

All of the information collected will be kept strictly confidential. You will be assigned a personal identification number, to ID all of your data. Your ID and personal data will be stored on the University of Prince Edward Island firewall protected secure server that is only assessable with password. Your anonymous response will not be associated with your personal data once testing is completed.

Results

If you so desire a summary of the findings from this research can be sent to you via email. Findings will be submitted for publication in peer reviewed ournals and present at academic and professional conferences.

If you have any questions or concerns please contact

Julia McKenna- Research Assistant- jpmckenna@upei.ca

Professor William J. Montelpare, Ph.D.,
Margaret and Wallace McCain Chair in Human Development and Health,
Department of Applied Sciences, Faculty of Science,
Health Sciences Building, University of Prince Edward Island,
550 Charlottetown, PE, Canada, C1A 4P3
(o) (902) 620-5186

Appendix C

Otological Normality Questionnaire

Participant's Name:
Participant's Surname:
Participant's ID:

Please Select your Varsity sport: Drop down menu

Participant's email

Otological History

Do you have any known hearing impairment? Y/N
Have you had any operations on your ears? Y/N
Do you have persistent tinnitus (ringing in ears)? Y/N
Do you have any problems with your balance? Y/N

Risk Factors
Have you had any exposure to loud sounds within the previous 48 hours (e.g. occupational, recreational, gunfire)? Y/N
Are you on any medication (ototoxic drugs)? Y/N
Have you any family history of hearing impairment? Y/N
How if your overall health? Very poor, Poor, Good, Excellent.

Otological Examination (performed with an otoscope)
Right EAM obstruction (e.g. wax, detritus, ++) _____
Left EAM obstruction (e.g. wax, detritus, ++)_____
Right Pinna (e.g. No Abnormality Detected: NAD) _____
Left Pinna (e.g. No Abnormality Detected: NAD) _____
Right Tympanic membrane (e.g. No Abnormality Detected: NAD) _____
Left Tympanic membrane (e.g. No Abnormality Detected: NAD) _____

OAE Section
SSOAE Right ear (Spontaneous otoacoustic emission) Y/N/Unsure
SSOAE Left ear (Spontaneous otoacoustic emission) Y/N/Unsure

Add Comments: _____

Appendix D

Depression Anxiety and Stress Scale-21

(Lovibond & Lovibond, 1995)

DASS 21	*Name:*	*Date:*

Please read each statement and circle a number 0, 1, 2 or 3 which indicates how much the statement applied to you *over the past week*. There are no right or wrong answers. Do not spend too much time on any statement.

The rating scale is as follows:

0 Did not apply to me at all
1 Applied to me to some degree, or some of the time
2 Applied to me to a considerable degree, or a good part of time
3 Applied to me very much, or most of the time

1	I found it hard to wind down	0 1 2 3
2	I was aware of dryness of my mouth	0 1 2 3
3	I couldn't seem to experience any positive feeling at all	0 1 2 3
4	I experienced breathing difficulty (eg, excessively rapid breathing, breathlessness in the absence of physical exertion)	0 1 2 3
5	I found it difficult to work up the initiative to do things	0 1 2 3
6	I tended to over-react to situations	0 1 2 3

7	I experienced trembling (eg, in the hands)	0 1 2 3
8	I felt that I was using a lot of nervous energy	0 1 2 3
9	I was worried about situations in which I might panic and make a fool of myself	0 1 2 3
10	I felt that I had nothing to look forward to	0 1 2 3
11	I found myself getting agitated	0 1 2 3
12	I found it difficult to relax	0 1 2 3
13	I felt down-hearted and blue	0 1 2 3
14	I was intolerant of anything that kept me from getting on with what I was doing	0 1 2 3
15	I felt I was close to panic	0 1 2 3
16	I was unable to become enthusiastic about anything	0 1 2 3
17	I felt I wasn't worth much as a person	0 1 2 3
18	I felt that I was rather touchy	0 1 2 3
19	I was aware of the action of my heart in the absence of physical exertion (eg, sense of heart rate increase, heart missing a beat)	0 1 2 3
20	I felt scared without any good reason	0 1 2 3
21	I felt that life was meaningless	0 1 2 3

Appendix E

Pain Anxiety Symptoms Scale-20

(McCraken and Dhingra, 2002)

	Never					Always
1. I can't think straight when in pain	0	1	2	3	4	5
2. During painful episodes it is difficult for me to think of anything besides the pain	0	1	2	3	4	5
3. When I hurt I think about pain constantly	0	1	2	3	4	5
4. I find it hard to concentrate when I hurt	0	1	2	3	4	5
5. I worry when I am in pain	0	1	2	3	4	5
6. I go immediately to bed when I feel severe pain	0	1	2	3	4	5
7. I will stop any activity as soon as I sense pain coming on	0	1	2	3	4	5
8. As soon as pain comes on I take medication to reduce it	0	1	2	3	4	5
9. I avoid important activities when I hurt	0	1	2	3	4	5
10. I try to avoid activities that cause pain	0	1	2	3	4	5
11. I think that if my pain gets too severe it will never decrease	0	1	2	3	4	5
12. When I feel pain I am afraid that something terrible will happen	0	1	2	3	4	5
13. When I feel pain I think I might be seriously ill	0	1	2	3	4	5
14. Pain sensations are terrifying	0	1	2	3	4	5
15. When pain comes on strong I think that I might become paralyzed or more disabled	0	1	2	3	4	5
16. I begin trembling when engaged in activity that increases pain	0	1	2	3	4	5
17. Pain seems to cause my heart to pound or race	0	1	2	3	4	5

18. When I sense pain I feel dizzy or faint	0	1	2	3	4	5
19. Pain makes me nauseous	0	1	2	3	4	5
20. I find it difficult to calm my body down after periods of pain	0	1	2	3	4	5

Appendix F

SAS Program for the Spearman Correlation Coefficient and Logistic Regression Analysis

(Montelpare, 2015)

```
options pagesize=55 linesize=135  date;
LIBNAME Julia '/home/montelpare/public_html/Julia';

data Julia.July06; set Julia.June15MRG;

ODS HTML BODY='july06reg-body.htm'
         FRAME='july06reg-frame.htm'
      CONTENTS='july06reg-contents.htm'
          PAGE='july06reg-page.htm';

proc sort data=Julia.July06 noequals; by id;
proc sort data=Julia.July06 noequals; by sex;

proc freq; tables Depress Stress cog escape fear physio
anxGroup; by sex;
proc sort data=Julia.July06 noequals; by sex;

proc logistic data=Julia.July06 descending;
class sex  / param=ref ; model escapeGroup   = lf hf lf_hf
rmssd mnhr sex/rsquare noint;
proc logistic data=Julia.July06 descending;
class sex  / param=ref ; model escapeGroup   = Y1414 SUM14
X2000 SUM20 DIF20  sex/rsquare noint;

proc logistic data=Julia.July06 descending;
class sex  / param=ref ; model cogGroup = lf hf lf_hf rmssd
mnhr sex/rsquare noint;
proc logistic data=Julia.July06 descending;
class sex  / param=ref ; model cogGroup = Y1414 SUM14 X2000
SUM20 DIF20  sex/rsquare noint;


proc logistic data=Julia.July06 descending;
class sex  / param=ref ; model depGroup = lf hf lf_hf rmssd
mnhr sex/rsquare noint;
```

```
proc logistic data=Julia.July06 descending;
class sex  / param=ref ; model depGroup = Y1414 SUM14 X2000
SUM20 DIF20  sex/rsquare noint;

proc logistic data=Julia.July06 descending;
class sex  / param=ref ; model strGroup = lf hf lf_hf rmssd
mnhr sex/rsquare noint;
proc logistic data=Julia.July06 descending;
class sex  / param=ref ; model strGroup = Y1414 SUM14 X2000
SUM20 DIF20  sex/rsquare noint;

proc logistic data=Julia.July06 descending;
class sex  / param=ref ; model fearGroup     = lf hf lf_hf
rmssd mnhr sex/rsquare noint;
proc logistic data=Julia.July06 descending;
class sex  / param=ref ; model fearGroup     = Y1414 SUM14
X2000 SUM20 DIF20  sex/rsquare noint;

proc logistic data=Julia.July06 descending;
class sex  / param=ref ; model anxGroup = lf hf lf_hf rmssd
mnhr sex/rsquare noint;
proc logistic data=Julia.July06 descending;
class sex  / param=ref ; model anxGroup = Y1414 SUM14 X2000
SUM20 DIF20  sex/rsquare noint;

proc logistic data=Julia.July06 descending;
class sex  / param=ref ; model physioGroup   = lf hf lf_hf
rmssd mnhr sex/rsquare noint;
proc logistic data=Julia.July06 descending;
class sex  / param=ref ; model physioGroup   = Y1414 SUM14
X2000 SUM20 DIF20  sex/rsquare noint;
/*
run;
ods html close;
 ods output close;
 ods listing;

run;
```